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BENIGN AND MALIGNANT CONDITIONS OF THE CERVIX UTERI.[1]

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CYCLICAL changes in the uterus have been recognized since the time when they were first demonstrated by Adler and Hitschmann[1] in 1907. It remained, however, for Allen and Doisy,[2] who followed up the work of Stockard and Papanicalou,[3] to demonstrate changes in the whole of the genital tract. Amongst the parts which pass through these regular changes, is the *cervix uteri*, and this organ undergoes considerable histological alteration, corresponding with ovulation, menstruation, and the effects of anterior hypophyseal secretions.

The effect of pituitary and ovarian secretions upon the cervix are modified still further by the interaction of these and other endocrine glands. The anterior pituitary action may be so great that, although in any normal pregnancy the luteal secretions inhibit œstrum, yet, as Loeser[4] has demonstrated, a condition of artificial ovulation may be produced by injecting anterior hypophyseal extracts into a pregnant animal.

Œstrin, which is the follicular hormone, produces considerable engorgement of the cervix, so much so that the squamous epithelium of the *portio vaginalis cervicis* becomes very much thickened, and sections taken at this time show squamous epithelium sixteen or more cells in thickness. At anœstrum the epithelium may be only four or five cells thick, and leucocytes are able to find their way through and become part of the vaginal secretion. For this reason the vaginal secretion at anœstrum contains many leucocytes and nucleated epithelial cells. At

[1] Read at a meeting of the South Australian Branch of the British Medical Association on November 24, 1932.

œstrum, however, the thick layers of cells impair the blood supply to the superficial cells, and their nuclei fade and the cells are desquamated, so that the vaginal secretion is now thick, and microscopy shows mainly cornified epithelial cells. The production of this latter state may result from anterior hypophyseal activity and over-secretion (or production of prolan *A* by the anterior pituitary lobe), or may be produced artificially by injection of an extract of the anterior pituitary lobe. It must be observed, however, that this will not result if the ovaries have been removed. Because of this fact (and in view of the fact that excess of prolan causes the production of follicular cysts of the ovary), it is considered that the follicular secretion is the cause of the cervical engorgement, although in this case the primary cause is the activity of the anterior hypophysis. This fact is significant in view of the work of Hofbauer,[5] who has artificially produced abnormal epithelial formations in the cervix by administering anterior pituitary lobe substances. He believes that this phenomenon has an important bearing upon the problem of the ætiology of carcinoma of the cervix.

The same worker[6] cites the case of *urethritis cystica*, which occurs in the trigone of the bladder and which so readily develops into a carcinomatous condition. Because the embryological origin of the bladder trigone and the cervix is mesodermal, Hofbauer considers it not unreasonable to ascribe malignant growth in these tissues to the operation of the same stimulus to hyperplasia, that is, excessive anterior pituitary hormone.

It will be remembered that the bladder trigone arises from the caudal end of the Wolffian duct, and the cervix from the caudal end of the Müllerian duct when these embryological structures fuse each with its fellow of the opposite side, owing to the rotation which occurs in the mesentery attached to the dorsal wall of the cœlom.

Conditions which are responsible for increasing anterior pituitary and ovarian activity may be pathological and physiological. These latter conditions include sexual relationships, which, in sexually excitable individuals, react very greatly upon hormonic secretions in addition to the local engorgement which is produced. When one adds to these contributing causes of cervical pathological change the effects of parturition, it will be readily understood why the *virgo intacta* is less liable to cervical malignancy than sexually functioning *multiparæ*.

We have made several hundred Aschheim-Zondek tests for pregnancy, and we have made over seventy œstrin tests during pregnancy. These tests were made according to the methods of Siddall. All biopsies of recent dates have been controlled by injections of urine into laboratory animals; the work has been spread over six years. There is no hasty conclusion about this work, and the cases here submitted are offered as a basis for increasing the early detection of cancer.

Infective Processes in the Cervix.

The commonest cause of cervicitis is the infective process invading lacerations of the cervix. Williams discusses five hundred consecutive deliveries, and he found that most of the women had considerable lacerations of the cervix. These patients sooner or later developed a mixed infection, which, as Schlink[7] and Young[8] have indicated, extends into the utero-sacral and other ligaments, and also produces general debility.

Next to these infections as a cause of cervicitis is the gonococcus, which, after the initial acute condition has abated, may remain latent, producing only some erosion and chronic cervicitis, which is so frequently and casually referred to as leucorrhœa, or "whites". There are cases of what Bailey[9] terms true erosion of the cervix in virgins, due to developmental anomalies, and upon which infective processes are planted, but these are rare. Any or all of the infective processes may be present in a latent condition, but as soon as the resistance is lowered by fatigue, illness or other debilitating cause, then the infective process bursts into activity. I have seen several patients who have been maligned by an accusation of gonorrhœal infection. They may have been referred for treatment on this account because the infection appears to be a recent one, and the failure to find *Diplococcus intracellularis* in a smear leaves an element of doubt. Nevertheless, many of these are old latent conditions which have only recently taken on fresh activity.

Cervical Pathological Change.

Bailey, who examined over eight hundred cervices in serial sections, has given a very clear picture of pathological conditions, especially when correlated with the work of Strachan,[10] Maryan,[11] Culbertson[12] and Charles Mayo.[13] Cervicitis begins either with infection which undermines the squamous epithelium, or with trauma at parturition, or operation. Whatever the original cause, the area around the *os externum* becomes denuded of its squamous epithelial covering, and a round cell infiltration occurs, and the infective process, which is at first progressive, finally reaches a stage when the irritation begins to subside. At first there are œdema and hyperæmia of the part; but subsequently the rapidly growing columnar epithelium of the endocervix spreads down over the desquamated area, and glandular elements dip down into the stroma and produce small glands which secrete freely (hence the mucopus at this stage). The cervix now appears through a speculum as a bulky organ with a very marked circum-oral redness (see Figure I).

Digital examination of the cervix reveals a velvety feeling to the touch and the tissues bleed easily. After this stage the slow-growing squamous epithelium grows over the new formed glands of the cervix and may seal off their mouths, so that the secretions are locked in, and hence small cysts or follicles develop, which are the *ovulæ Nabothi* (Figures I and II). Cyclic changes and hormonic stimuli *plus* other irritation may ultimately develop carcinogenic tissue in the cervix.

It is significant that over 90% of cases of cancer of the cervix occur in parous women. De Lee says that he has not seen cancer of the cervix when immediate repair has been effected *post partum*, and this belief led him to coin the phrase *restitutio ad integram*.

FIGURE I.
Photograph of section of uterus. *Ovulæ Nabothi* of *cervix uteri* shown in uterine section.

Treatment of Cervical Lesions.

Prophylaxis in the form of immediate suture, as advised by De Lee,[14] is the greatest eradicator of causes of pathological change of the cervical tissues. My methods of treatment of cervicitis include irrigation, topical applications of solutions, such as mercurochrome and acriflavine, and also submucous injections of similar agents.[15][16]

Medical diathermy, with which I also dealt, has been fully discussed in many journals. It is essential that the active electrode should be maintained at a strictly regulated temperature. I have performed coagulation of the cervix by diathermy in nearly five hundred cases, and the results obtained have been most encouraging, while, in addition, the patients appreciate the ambulatory method of treatment. After exposure of the cervix by means of a bivalve speculum, the organ is cleaned with alkaline solutions and Ryall's cocaine solution is applied with cotton wool on wooden applicators plugged into the cervical canal, while others are applied to the eroded part of the *portio vaginalis cervicis*. After a short time the application is removed, and, working from within out, the eroded surface is coagulated with a fine active electrode; the inactive electrode of limpet metal encircles the body of the patient. The cervix is thus coagulated with linear striæ in a manner which gives the appearance of the spokes of a wheel.

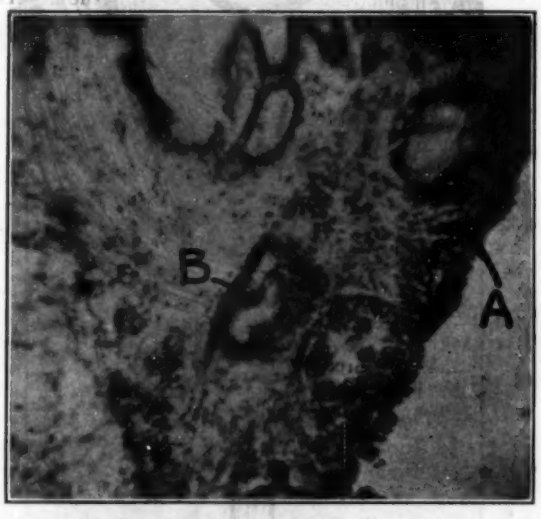

FIGURE II.
Photomicrograph of early *Ovulæ Nabothi*. A = squamous epithelium, B = one of early Nabothian follicles.

Several cervices have been drawn for me by Mr. Hendrickson, in phases immediately before, immediately after, and some time after coagulation. These drawings are shown here (Figures III and IV).

The scar tissue which results from the coagulation develops as connective tissue, which destroys the remaining columnar epithelium, and the squamous epithelium gradually covers over the fibrosed area. Any Nabothian follicles are destroyed by ignipuncture before the surface coagulation takes place.

The electric cautery is used in much the same way, but I have used it usually while the patient is under general or spinal anæsthesia. The great point to be observed with the electric cautery is that if the cautery be hotter than dull red heat, there is a tendency to subsequent hæmorrhage.

The destruction of Nabothian follicles high up in the cervical canal is better affected by diathermy.

Trachelorrhaphy.

Trachelorrhaphy is instituted to repair a lacerated cervix which has become infected. There are

large discharging surfaces and these are considered to affect the general health, much as septic tonsils do, although my experience is that the closed infections are more important as the cause of general indisposition than are those of open cervical

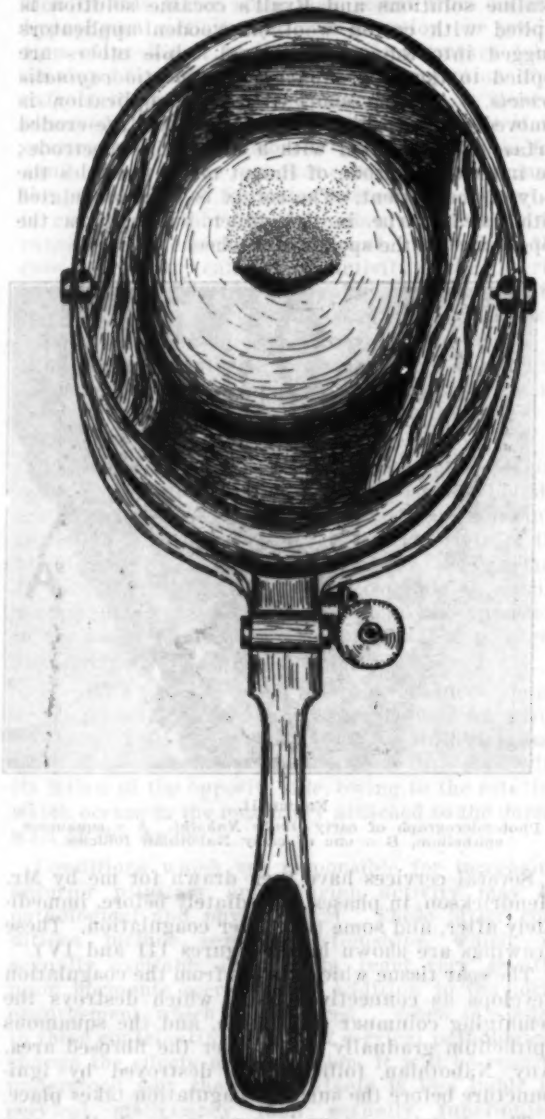

FIGURE III.
Drawing of early simple erosion.

erosions. The infected surfaces are dissected off and the raw areas approximated with chromicized catgut (Figures V and VI). If a deeper infection or stellate laceration exists (Figure VII), the Sturmdorf amputation should be done or Schlink's enucleation operation may be performed.

Premalignant and Malignant Conditions of the Cervix.

If De Lee's statement about the suture of torn cervices be true, then we must regard the interregnum phases between laceration and cancer as being premalignant. References are numerous concerning the inception of cervical carcinoma in *multiparæ* relative to its occurrence in *nulliparæ*, the former being over 90%. Over a period of some

FIGURE IV.
Drawing of radial coagulation of cervix by diathermy.

years I have examined cervical sections and have recognized no half-way stage between non-malignancy and cancer, although one does appreciate the conception of premalignancy clinically. Dr. Bull, who has examined many hundreds of sections, says that he has not yet seen a line of transition in cervical pathological change, as is the case in other parts of the body. Bailey,[18] however, states that "the ultimate sequel to erosion

is malignancy", and he does actually indicate the presence of some stage of pathological transition (Figures VIII and IX).

FIGURE V.

Illustrating method of inserting invaginating sutures in Sturmdorf's operation (after Polak). (Reproduced from an article by H. H. Schlink, THE MEDICAL JOURNAL OF AUSTRALIA, June 7, 1924.)

In the case of Mrs. J., whom I regarded as having a possibly malignant cervix, I made sections in which no evidence of malignant change could be found (Figure X). However, I used Hofbauer's method of injecting urine from this patient into laboratory animals, and obtained

FIGURE VI.

Showing mattress sutures in Sturmdorf's operation. The anterior suture is drawn taut and not tied. In the lower suture this has not been done (after Polak). (Reproduced from an article by H. H. Schlink, THE MEDICAL JOURNAL OF AUSTRALIA, June 7, 1924.)

a positive result in the ovaries as well as cervical hyperplasia. Biopsy was again made later, and the cervix of the patient was found to be the seat of malignant epithelial hyperplasia, and I performed Wertheim's radical panhysterectomy with removal of cellular tissue and glands (Figure XI).

Hofbauer's work was based on the Aschheim-Zondek test, which is positive in some cases in cancer of the cervix. Hofbauer has actually produced cervical epitheliomata in rats by giving large doses of anterior pituitary extract. I have examined the urine of women in what were regarded as premalignant and malignant states of the cervix. I found that tests made with urine from the malignant cases resulted in follicular ripening in the ovaries of the test animals. Some of the cases which were clinically regarded as premalignant, but pathologically benign, gave similar positive results to the tests.

FIGURE VII.

Photograph of slide of whole uterus. The cervix shows cervical infection from *portio vaginalis* to the internal os.

Mrs. J., for example, gave a positive reaction for cervical malignant disease, when biopsy revealed no such state. Later, however, in six months, the biopsy showed the existence of a frankly malignant condition of the cervix. Although one swallow does not make a summer, it indicates a change of season.

Another patient, Mrs. D., had macroscopical premalignant disease of the cervix, but biopsy showed a benign condition (see Figure II). Because of former experience, I did a total hysterectomy, and the result has been quite satisfactory.

This, of course, is a case of "not proven", but I display here the animals used, and it is easy to compare the controls with the two injected animals (Figure XII). The photograph (Figure XIII) is the result of injections of urine intravenously into a segregated test rabbit in accordance with the work of Friedman and Lapham.[21] Since this has been my experience in a number of cases, I have felt more than justified in removing the whole uterus and cervix when formerly I should have made a subtotal hysterectomy. This method of treatment has the support of Masson,[22][23] of the Mayo Clinic, who does less than 10% subtotal hysterectomies; also

FIGURE VIII.
Photograph of slide of carcinoma of cervix.

of Spirito,[24] who either does a total hysterectomy, or amputates the cervix as a prophylaxis against cancer. Masson writes:

> The reduced blood supply of the cervix after subtotal hysterectomy starts degenerations and lowered resistance; this leads to a focus of infection.

Schlink, with the same idea in mind, uses his enucleator to core out the cervix, either from the abdominal or from the vaginal aspect.

Conservative gynæcologists, like Cuthbert Lockyer, are now protagonists of total hysterectomy. In Sydney there is general approval of the total hysterectomy. Schlink has given me information regarding the morbidity of the cervical stump and the inception of cancer, which he has collected, which is astounding. These reports will be published later. Maguire also has been able to show

FIGURE IX.
Photomicrograph of cancerous cells invading the cervical tissue.

a large, or relatively large, number of cases of the occurrence of malignant disease in the cervical stump. Charles Mayo has collected 99 cases, J. O. Polak 250 cases, Fleischmann 50 cases, Sanders 102

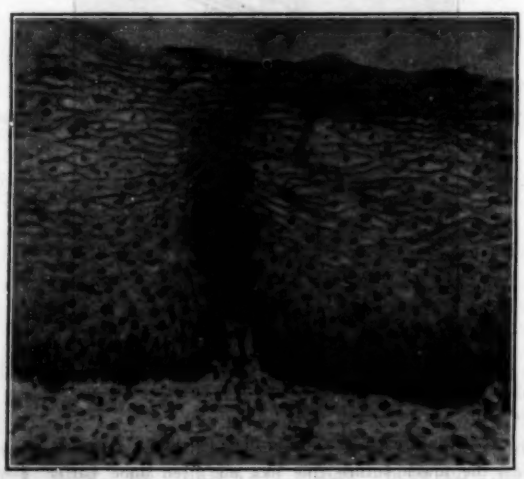

FIGURE X.
Photomicrograph of cervical tissue from Mrs. J. This was quite benign, though the squamous layers were very thick.

cases, and there are many others. It has been calculated that the occurrence of cancer in the cervical stump is over 6%, whereas it was thought to be about 0·5%.

In some cases of what appeared to be premalignant cervicitis, in which there were big, bulky cervices, I have coagulated the erosion and then inserted a halo of needles round the cervix, the radiation being filtered through 0·5 millimetre of platinum. The cervix received about eight hundred milligramme-hours of radium, and Fowler[25] has shown his practical approval of the method by subsequently following the same lines of treatment.[1]

FIGURE XI.

Photomicrograph of cervical tissue from Mrs. J. The condition is here seen to be malignant.

The Treatment of Cancer of the Cervix.

When a cervical biopsy shows an invasion of the cellular tissues by malignant epithelial tissue, the outlook is very grave, and the means of combating the carcinomatous growth are somewhat limited. The treatment is one of three types: (i) Wertheim's radical panhysterectomy (if the case be operable), (ii) radium treatment both for operable and inoperable cases, (iii) radium and X ray treatment combined.

The first method may advantageously be combined with pre-operative irradiation. The methods which I prefer are a combination of pre-operative irradiation and Wertheim's radical operation. Maguire and Schlink, of Sydney, both working in separate groups, have come to regard pre-operative irradiation as a very great asset in the radical hysterectomy. The irradiation is made a week or two beforehand, but not long enough to produce that severe fibrosis which interferes with operative manœuvres. The field is irradiated for about three thousand milligramme-hours. This preliminary irradiation improves any secondary infective condition, and it provides secondary radiation, which extends into the tissues and tends to destroy any remaining cancer cells in the pelvic lymphatics *et cetera*.

The actual operative technique followed is that of Bonney,[26] because Bonney has had greater success with his wide excision than has been obtained by any other individual or by any other means. The dexterity of Bonney is the result of practice in about six hundred cases, and of his remarkable surgical skill. Because of this, his results must not be accepted as being applicable to every surgeon. Heyman[27] comes next in this field, and his patients are all treated by radium, and in some instances combined with X ray cross-fire. The obvious advantage of radium treatment is that it does not require the same degree of skill as is necessary for a Wertheim type of operation, and, further, that any patient, whether her condition be operable or inoperable, can have treatment. In some cases, initially considered inoperable, radium treatment has enabled operative treatment to be instituted.

The methods of treatment vary and the results vary likewise, but apart from this it is difficult to obtain satisfactory comparisons because, even though the cases are all subjected to biopsy, yet the very early carcinomata are almost as amenable to treatment as is a late case of cervical erosion which is shown to be premalignant by animal test. Methods which have met with fairly satisfactory results are: (i) The insertion of two capsules of radium, containing fifty milligrammes each, the radiation being filtered through one millimetre of platinum and further screened by rubber tubing. These are inserted into the uterine cavity and cervical canal in tandem and retained there by suture. (ii) There is also a cross-fire method by which emanations from radium needles placed around the periphery of the cervix are

FIGURE XII.

Photographs of ovaries removed from animals used in the investigations.

[1] At this stage a moving picture of Dr. Matters was shown doing a total hysterectomy with the aid of a Maguire retractor.

used, the needles being inserted with their points directed inwards. Some 7,000 milligramme-hours are given. This method, used by Curtis, is not used much now. (iii) Another method which has met with some measure of success is that fostered by Donaldson. It is applicable to cases in which the broad ligaments have been invaded. Capsules of fifty milligrammes, either singly or in tandem, are placed in the uterus. Now the abdomen is opened and a stab wound is made near each anterior superior iliac spine and a track is made down to the broad ligament. A fine rubber tube, with 25 milligrammes of radium in the lower end, is guided down the track with a long Spencer Wells curved forceps. This is done on either side and the abdomen is closed. If the radium be adequately screened, about eight thousand milligramme-hours are given. This has been used in inoperable cases.

A method which is used abroad, but which we have not embarked upon, is the cross-fire between implanted radium and X radiation. The results do not appear to warrant the disturbance so often caused to the patient by X ray treatment. The Paris method of intrauterine capsules of radium with a radium colpostat has produced results which have given a considerable degree of satisfaction, especially to Regaud. There is finally the method of total excision followed by irradiation of the iliac glands by X rays after the operation. My own leanings with regard to these conditions depend upon: (*a*) the degree of invasion and the mobility of the uterus; (*b*) the fatness of the patient, having in mind the necessary manipulations through the abdominal wall; (*c*) the general condition of the patient with regard to anæmia *et cetera*. In point of fact, I prefer the method of excision preceded by radium treatment in all suitable cases. I try to reduce the shock of prolonged anæsthesia by using spinal anæsthesia for the first hour or more, if possible, and by giving pituitrin and a hypertonic solution of glucose to prevent capillary stagnation of the blood, and to avoid fluid loss from the blood stream into the tissues.

When the case is unsuitable, even in very advanced conditions, radium is used, and it is generally conceded, as Ward and Farrar pointed out, that even though no cure results, the comfort of the patient, even by the reduction of the offensive odour, is greatly benefited.

FIGURE XIII.
Showing animals used in some of the tests.

Acknowledgements.

I desire to convey my thanks to Dr. Bull, pathologist of the Adelaide Hospital, and to Dr. Rica Hübbe, for the great help that they have given me with sections *et cetera*.

The animal investigation work was carried out in the Department of Physiology and Pharmacology in the University of Adelaide, to which I am grateful for the provision of such valuable aids to clinical research.[1]

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THE EFFECT OF MOLYBDENUM IMPURITY IN THE ARSENOPHOSPHOTUNGSTIC ACID REAGENT ON THE URIC ACID CONTENT OF BLOOD.

By VERA I. KRIEGER, M.Sc.

(From the Biochemistry Department, University of Melbourne, and the Women's Hospital, Melbourne.)

In an investigation of the chemistry of the blood in toxæmias of pregnancy, in normal pregnancy and in normal non-pregnant individuals,[1] uric acid values were found to be higher than those reported in the literature. Table I indicates the range of values obtained in the various conditions studied, when the direct method of Benedict[2] was used.

In order to determine the reason for this discrepancy, a comparison was made of various methods in general use.

When uric acid was estimated in the same specimen of blood by the Benedict direct method[2] or by the Folin and Wu direct method[3] with the Folin and Trimble[4] phosphotungstic acid reagent, comparable results were obtained, whereas with the Morris and Macleod method[5] the values were consistently lower. The Folin and Wu method was, however, found to be unsatisfactory since, in many cases, a precipitation occurred before the colorimetric comparison could be made.

TABLE I.

Condition.	Number of Cases.	Maximum.	Minimum.	Average.
Normal (non-pregnant)	38	8·3	5·6	7·1
Normal (pregnant)	11	9·5	4·8	7·1
Pyelitis	8	7·5	4·6	6·2
Slight albuminuria	11	9·1	2·7	7·0
Albumin of labor	6	11·0	2·6	6·7
Hyperemesis	8	8·9	4·6	7·6
Hæmorrhage	4	8·9	5·5	6·9
Nephritis	13	11·8	4·8	8·4
Eclampsia	21	10·3	5·8	8·0
Pre-eclampsia	43	13·2	3·7	7·8

With the Morris and Macleod method of estimation the blue colour was very pale, and this led to difficulty in comparing the unknown with the standard. Tables II and III show comparisons of values obtained with these methods.

TABLE II.

Benedict Method. Milligrammes of Uric Acid per 100 Cubic Centimetres of Blood.	Folin Method. Milligrammes of Uric Acid per 100 Cubic Centimetres of Blood.	Difference.	Percentage Difference.
5·4	5·8	0·4	7·5
5·7	5·9	0·2	3·5
6·0	5·7	0·3	5·0
6·2	7·7	1·5	25·0
6·2	5·9	0·3	3·5
6·3	5·4	0·9	14·0
6·7	8·3	1·4	21·0
6·8	6·5	0·3	4·0
6·9	5·8	1·1	16·0
7·3	7·0	0·3	4·0
7·8	8·2	0·6	6·6
8·2	8·9	0·7	8·5
8·9	9·4	0·5	5·6
9·0	9·9	0·9	10·0

TABLE III.

Benedict Method. Milligrammes of Uric Acid per 100 Cubic Centimetres of Blood.	Morris and Macleod Method. Milligrammes of Uric Acid per 100 Cubic Centimetres of Blood.	Difference.	Percentage Difference.
3·8	1·8	2·0	53
3·9	2·9	1·0	25
3·9	2·0	1·9	49
3·9	2·0	1·9	49
4·2	1·7	2·5	60
4·2	3·2	1·0	24
4·3	2·2	2·1	50
4·6	2·6	2·0	43
4·8	2·2	2·6	54
4·9	2·8	2·1	43
4·9	3·1	1·8	46
5·6	4·3	1·3	23
6·7	6·0	0·7	10
6·6	4·0	2·6	39
8·3	5·4	2·9	35
8·8	5·0	3·8	43
8·8	4·8	4·0	91

Adjustment of Reagents.

It has been reported by Pucher[6] that care must be taken to adjust the two-thirds normal sulphuric acid used in precipitating the protein from the blood so that it is exactly equivalent to the sodium tungstate used. A series of estimations comparing

the value for the uric acid present when two-thirds normal sulphuric acid was used in the protein precipitation and when adjusted sulphuric acid was used showed practically identical results.

TABLE IV.

Blood Specimen Number.	Precipitating Agent: 1 volume of two-thirds normal Sulphuric Acid and 1 volume 10% Sodium Tungstate.	Precipitating Agent: 1 volume of Sulphuric Acid = Sodium Tungstate and 1 volume 10% Sodium Tungstate.
1	7·8 mgms. per 100 c.cms. blood	7·2 mgms. per 100 c.cms. blood
2	7·6 mgms. per 100 c.cms. blood	7·2 mgms. per 100 c.cms. blood
3	7·6 mgms. per 100 c.cms. blood	7·4 mgms. per 100 c.cms. blood
4	7·6 mgms. per 100 c.cms. blood	7·2 mgms. per 100 c.cms. blood
5	7·6 mgms. per 100 c.cms. blood	7·4 mgms. per 100 c.cms. blood
6	7·1 mgms. per 100 c.cms. blood	7·0 mgms. per 100 c.cms. blood
7	6·8 mgms. per 100 c.cms. blood	6·4 mgms. per 100 c.cms. blood

Age of Reagents.

It has been stated that the sodium cyanide used in the estimation should be at least two weeks old. Comparisons were made, freshly prepared cyanide, cyanide about two weeks old, and cyanide at least three months old being used. The results obtained were identical with all samples.

Purity of Reagents.

The purity of the uric acid used for making the standard uric acid solution was tested by determination of the nitrogen content by the Kjeldahl method. The theoretical and experimental figures were in agreement.

Chemicals obtained from the Dunn Laboratory, Saint Thomas's Hospital, London, were used in the preparation of a Benedict uric acid reagent. On comparing the blue colour developed in a standard uric acid solution when this reagent was used, with that developed in the same solution when the original Benedict reagent was used, a marked difference was observed. This difference was so great as to make the two solutions quite incomparable in the colorimeter. The colour developed with the reagent prepared in Australia was purplish-blue, while that prepared at Saint Thomas's Hospital was pure blue.

The determination of the uric acid content of a series of blood filtrates when the Australian reagent was used in both standard and unknown solutions, and the comparison with the uric acid content when the English reagent was used in standard and unknown, indicated that higher values were always obtained with the Australian reagent.

Reagents were made, each of the chemicals procured in Australia being substituted, in turn, for one of those in the English reagent, and only when the sodium tungstate procured in Australia was used did the purplish-blue colour develop.

The fact that the purplish-blue colour developed in the standard as well as in the unknown when the Australian tungstate was used, and also that the uric acid content of the blood was always higher when this reagent was used, seems to indicate that there was some impurity in the sodium tungstate which was capable of interacting with some substance or substances present in the blood.

An attempt was made to purify the sodium tungstate procured in Australia by recrystallization from water and by extraction with alcohol. Reagents prepared with each of these samples of purified sodium tungstate gave results identical with those given when the reagent made with the original sodium tungstate was used.

It has been reported by Folin and Trimble[7] that molybdenum impurity in the sodium tungstate caused interference in the uric acid estimation. They developed a method for the detection of molybdenum by means of potassium xanthate, and also a method of preparing a reagent from sodium tungstate containing molybdenum. Each of the samples of sodium tungstate was tested for molybdenum. A reagent was prepared from the original sample of sodium tungstate, a modification of the method for precipitation of the molybdenum by hydrogen sulphide, as described by Folin and Trimble, being used.

Uric acid reagents were also made from a number of different preparations of sodium tungstate. Uric acid was estimated in several blood filtrates, each of the reagents being used in turn on each specimen of blood.

In Table V are summarized the comparative uric acid values in four different specimens of blood, with the various reagents prepared, and the presence of molybdenum impurity and the reaction of the sodium tungstate in each reagent used are correlated.

TABLE V.

Source of Sodium Tungstate.	Sodium Tungstate Number.	Specimen of Blood. 1	2	3	4	Potassium Xanthate Test.	Reaction of Tungstate.
Mercks (A) (original used).	1	3·5	4·8	5·1	4·7	Large amount molybdenum.	Alkaline.
Mercks (recrystallized from water).	5	3·6	4·8	5·1	4·0	Large amount molybdenum.	Faintly alkaline.
Mercks (recrystallized from alcohol).	8	3·9	4·8	5·0	4·7	Large amount molybdenum.	Neutral.
British Drug House (A).	2	3·2	4·4	4·9	4·5	Definite molybdenum.	Definitely alkaline.
British Drug House (B).	9	2·9	4·1	4·6	4·0	Trace molybdenum.	Faintly alkaline.
British Drug House (C)	11	2·3	no	colour		No molybdenum.	Neutral.
Hopkins and Williams (A).	6	2·5	4·4	4·7	4·2	Definite molybdenum.	Alkaline.
Hopkins and Williams (B) (used in England)	3	2·2	4·2	4·7	3·8	Molybdenum.	Alkaline.
Hopkins and Williams (B) (used with Australian chemicals).	4	2·2	4·1	4·6	4·4	Molybdenum.	Alkaline.
Bakers.	10	1·8	4·1	4·5	3·9	Molybdenum.	Definitely alkaline.
Mercks (B).	7	1·8	3·8	4·3	3·6	No molybdenum.	Strongly alkaline.
Mercks (A) (H_2S precipitation of molybdenum).	12	—	4·1	4·6	3·9	—	—

From these figures it seems certain that when molybdenum is present in the sodium tungstate used in the reagent, a high result is obtained. Folin[8] states that the sodium tungstate used should be readily soluble and alkaline to phenolphthalein. The lowest results were obtained with sodium tungstates free from molybdenum and with a markedly alkaline reaction to phenolphthalein. The original sodium tungstate was definitely alkaline, but con-

tained much more molybdenum than any of the other samples tested.

Relation Between Molybdenum Impurity in the Reagent and Thioneine in Blood in Producing High Uric Acid Values.

In 1929, Benedict, Newton and Behre[8] reported the presence of thioneine (thiasine) in blood, and showed that this substance interfered with the direct method of determining the uric acid content of blood. This substance could be precipitated with uric acid by the addition of silver lactate.

The silver urate was removed by treatment with 10% sodium chloride in one-tenth normal hydrochloric acid. The thioneine residue was readily soluble in sodium cyanide.

A series of estimations were made in which comparison was made of the uric acid in blood, as determined by the direct method, with the uric acid when determined by precipitation with silver lactate and extraction with 10% sodium chloride in one-tenth normal hydrochloric acid. The residue after this treatment was dissolved in sodium cyanide and the thioneine was determined as colour equivalent to uric acid. The sum of the indirect uric acid value and of the thioneine estimated as uric acid was greater than the uric acid determined by the direct method in 80% of the blood specimens examined.

From Table VI it is evident that, with thioneine (expressed as uric acid) above 1·7 milligrammes, there is a marked difference between the uric acid values determined by the direct and indirect methods, the discrepancy apparently being due to the amount of thioneine present in the blood, and its interaction with some constituent of the arsenophosphotungstic reagent with the production of a blue colour.

TABLE VI.

Blood Number.	Uric Acid from Thioneine.	Uric Acid from Thioneine Indirect.	Indirect Method.	Direct Method.	Direct Indirect Method.
5	1·2	4·5	3·3	4·2	0·9
6	1·3	4·8	3·5	4·3	0·8
2	1·4	5·0	3·6	4·0	0·4
13	1·4	5·3	3·9	4·7	0·8
33	1·5	11·2	9·7	9·4	0·3
22	1·6	6·6	5·0	5·8	0·8
14	1·6	5·9	4·3	4·7	0·4
10	1·6	5·1	3·5	4·4	0·9
8	1·6	4·5	2·9	4·4	1·5
4	1·7	5·6	3·9	4·1	0·2
11	1·7	5·3	3·6	4·5	0·9
12	1·7	5·4	3·7	4·6	0·9
15	1·7	4·8	3·1	4·8	1·7
18	1·7	5·7	4·0	5·0	1·0
32	1·7	13·5	11·8	8·8	3·0
31	1·8	8·5	6·7	8·8	2·1
30	1·8	10·9	9·1	8·3	0·8
27	1·8	6·6	4·8	6·6	1·8
9	1·9	4·9	3·0	4·4	1·4
17	1·9	5·9	4·0	4·9	0·9
28	1·9	6·9	5·0	6·7	1·7
1	2·0	4·8	2·8	3·7	0·9
3	2·0	4·7	2·7	4·0	1·3
16	2·0	5·5	3·5	4·9	1·4
19	2·0	6·0	4·0	5·2	1·2
29	2·0	7·1	5·0	7·7	2·0
20	2·0	5·3	3·3	5·3	2·0
23	2·1	7·0	4·9	6·0	1·1
21	2·1	5·8	3·6	5·3	1·7
25	2·2	6·0	3·8	6·6	1·8
7	2·3	6·4	4·1	4·3	0·2
26	2·4	6·4	4·0	6·6	2·6
34	2·4	12·5	10·1	10·7	0·6
24	3·0	6·6	3·6	6·5	2·9
35	3·1	11·3	8·2	10·3	2·1

Benedict and Newton[9] reported that on precipitation of protein with different samples of sodium tungstate, varying amounts of thioneine were present in the filtrate. They also reported one sample of sodium tungstate with which all the thioneine was precipitated.

Benedict and Newton[9] used molybdic acid dissolved in caustic soda, diluted with an equal volume of four-tenths normal sulphuric acid, for the protein precipitation, and stated that all the thioneine originally present in the blood was obtained in the filtrate, and consequently the uric acid value was higher than when sodium tungstate and sulphuric acid were used as precipitating agent.

It was therefore necessary to determine whether the molybdenum impurity in the tungstate used for precipitating the protein, or the molybdenum in the colour-developing reagent, was responsible for the high uric acid values, or both factors contributed to the discrepancy.

From the results tabulated in Tables VII and X, it seems certain that the sodium tungstate used as part of the protein precipitant has little or no effect on the amount of thioneine in the protein-free filtrate, and that there is no increase in the amount of thionine present in the filtrate when the tungstomolybdic acid protein precipitant is used.

The sodium tungstate in the arsenophosphotungstic acid reagent, however, causes marked variations in the uric acid values obtained for the same specimen of blood, dependent on the amount of molybdenum impurity present in it. The highest results were obtained with reagents number 1 and number 2, which were prepared from sodium tungstates containing large amounts of molybdenum impurity, whilst the lowest results were obtained with reagent number 7, containing molybdenum-free sodium tungstate.

Effect of Addition of Molybdate to Reagent Containing Molybdenum-Free Sodium Tungstate.

An arsenophosphotungstic acid reagent was prepared, sodium tungstate number 7 (molybdenum-free), sodium molybdate, arsenic oxide, and phosphoric acid being used, and the mixture being boiled for twenty minutes in the usual way. This reagent was termed *7b*.

Colour was developed in two five cubic centimetre portions of the diluted uric acid standard solution with (*a*) number 7 reagent, in which case a pure blue colour developed, and with (*b*) number *7b* reagent, the colour here being purplish-blue and similar to that developed when any of the reagents were used, in which the sodium tungstate had been shown to contain molybdenum impurity.

Removal of Molybdenum Impurity.

The method of Folin and Trimble,[4] already referred to, for preparing a molybdenum-free reagent by precipitation with hydrogen sulphide is very slow, and there is no means of testing when precipitation is complete.

An arsenophosphotungstic acid reagent was prepared, the appropriate amount of molybdenum-free

tungstic acid (the yellow anhydrous form) dissolved in the minimum amount of normal caustic soda, in place of the usual sodium tungstate, being used (number 13, Table VIII). Uric acid determinations on the same blood filtrate with this reagent and with reagent number 7 (molybdenum-free) agreed closely, whereas the value was definitely higher when the reagent subjected to hydrogen sulphide precipitation was used.

TABLE VII.

Tungstate for Precipitating Protein.	Tungstate in Arsenophospho-tungstic Acid Reagent.	Blood Number 1. Milligrammes of Uric Acid per 100 Cubic Centimetres of Blood.	Blood Number 2. Milligrammes of Uric Acid per 100 Cubic Centimetres of Blood.
No. 1	No. 1	—	5·2
No. 2	No. 2	4·6	5·3
No. 6	No. 6	4·9	5·4
No. 7	No. 7	3·0	2·6
No. 10	No. 10	3·2	3·9
No. 1	No. 2 (Molybdenum Impurity)	4·3	
No. 2	No. 2 (Molybdenum Impurity)	4·7	
No. 6	No. 2 (Molybdenum Impurity)	4·5	
No. 7	No. 2 (Molybdenum Impurity)	4·0	
No. 10	No. 2 (Molybdenum Impurity)	4·6	
Molybdo-sulphuric Reagent	No. 2	4·5	
No. 1	No. 1 (Marked Molybdenum Impurity)		4·9
No. 2	No. 1 (Marked Molybdenum Impurity)		4·7
No. 6	No. 1 (Marked Molybdenum Impurity)		4·9
No. 7	No. 1 (Marked Molybdenum Impurity)		4·9
No. 10	No. 1 (Marked Molybdenum Impurity)		
Molybdo-sulphuric Reagent	No. 1 (Marked Molybdenum Impurity)		
No. 1	No. 7 (Molybdenum Free)	2·7	2·5
No. 2	No. 7 (Molybdenum Free)	3·5	2·6
No. 6	No. 7 (Molybdenum Free)	3·0	2·2
No. 7	No. 7 (Molybdenum Free)	3·2	
No. 10	No. 7 (Molybdenum Free)	3·0	1·9
Molybdo-sulphuric Reagent	No. 7 (Molybdenum Free)	3·0	
Molybdo-sulphuric	No. 1	4·7	
Molybdo-sulphuric	No. 2	4·9	
Molybdo-sulphuric	No. 7	3·2	
Molybdo-sulphuric	No. 10	3·6	
No. 7 Molybdenum Free.	No. 1 Marked Molybdenum Impurity.	4·9	

An attempt was therefore made to prepare from sodium tungstate, shown to contain molybdenum, yellow, anhydrous tungstic acid, free from molybdenum. The following method proved satisfactory. Sodium tungstate was dissolved in a large amount of water in a one litre flask. Concentrated sulphuric acid was run into the solution from a dropping funnel till no further precipitation of the yellow, anhydrous tungstic acid took place. The mixture was transferred to a large beaker, stirred thoroughly and allowed to stand. The heavy, flocculent precipitate readily settled, and the supernatant fluid was decanted off. The precipitate was washed three times by decantation with large volumes of distilled water. The tungstic acid was then dissolved in a minimum amount of 40% caustic soda and diluted with an equal volume of water. The solution appeared to be faintly blue in colour, and a small amount of insoluble white residue remained. The solution was filtered, and a clear, colourless filtrate was obtained.

The filtrate was treated with concentrated sulphuric acid, the yellow precipitate was allowed to settle, and the supernatant fluid was decanted off. The precipitate was washed three times by decantation with large volumes of water. This procedure was important, since certain concentrations of sodium sulphate seemed to inhibit the precipitation of the tungstic acid.

The precipitate was again dissolved in soda, filtered, reprecipitated, and washed until it no longer gave a positive result for molybdenum when tested with potassium xanthate.

The molybdenum-free precipitate was transferred to an evaporating basin and dried in a current of warm air. The resulting lumps were ground to a fine powder and finally dried in an incubator at 37° C. The yield of tungstic acid obtained by this procedure was about 70% of the weight of the original sodium tungstate used.

An arsenophosphotungstic acid reagent was made with this purified tungstic acid dissolved in a minimum amount of normal sodium hydroxide (number 14, Table VIII).

TABLE VIII.

Reagent No. 7 Molybdenum-free Sodium Tungstate.	Reagent No. 13 Molybdenum-free Tungstic Acid in Normal Sodium Hydrate.	Reagent No. 14 Molybdenum-free Tungstic Acid from Molybdenum containing Sodium Tungstate in Normal Sodium Hydrate.	Reagent No. 12 Molybdenum precipitated by Sulphuretted Hydrogen.	Reagent No. 1 Sodium Tungstate containing Marked Molybdenum Impurity.
4·7	4·7		5·0	6·2
2·3	2·9			4·3
5·3	5·3	5·3		6·0
4·8		5·2	5·4	5·5
5·7		6·6	6·9	8·9
5·8		6·7	6·4	7·4
5·4	5·5	5·6	5·9	6·2
4·8	4·9	5·1	5·9	6·0

From Table VIII it is evident that in all cases molybdenum-free reagents give lower results than reagents containing molybdenum impurity. The reagent containing tungstic acid, prepared from sodium tungstate with a large amount of molybdenum impurity, gave results agreeing more closely with those when reagent number 7 (molybdenum-free) was used, than those obtained by using a reagent purified by hydrogen sulphide precipitation.

The effect of using larger quantities of arsenophosphotungstic reagent was tested with: (*a*) reagent containing molybdenum-free sodium tungstate, and (*b*) reagent containing a marked amount of molybdenum impurity.

The colour developed when one cubic centimetre of arsenophosphotungstic reagent containing molybdenum impurity was used, is thus not the maximal colour capable of being developed by the uric acid and thioneine present in the blood filtrate.

TABLE IX.

Specimen.	Cubic centimetres of Reagent Used.	Reagent No. 7 (Molybdenum-free). Milligrammes of Uric Acid in one hundred cubic centimetres of Blood.	Reagent No. 1. (Marked molybdenum impurity). Milligrammes of Uric Acid in in one hundred cubic centimetres of Blood.
Blood No. 1	1	3·1	4·4
	2	3·2	5·1
	3	3·7	4·2 (approx. only).
Blood No. 2	1	3·0	4·2
	2	3·4	5·8
	3	3·9	Colour very intense and difficult to compare with standard.

Nature of the Compound Producing Alteration in the Colour Development.

Although the Benedict reagent was an arsenophosphotungstic complex, and the Folin reagent a phosphotungstic complex, each gave high values for uric acid when molybdenum impurity was present, whilst the Morris and Macleod reagent, an arsenotungstic derivative, gave consistently low values. There is, therefore, reason to believe that some relationship exists between the phosphoric acid and the molybdenum impurity present in the sodium tungstate, and this complex is responsible for the alteration in colour when such a reagent is used.

It was also evident that the discrepancy between the uric acid values when molybdenum-free or molybdenum-containing arsenophosphotungstic acid reagents were used, was due to some substance or substances in the blood. After precipitation with silver lactate and extracting the resultant precipitate with 10% sodium chloride in one-tenth normal hydrochloric acid, the residue, containing thioneine and possibly glutathione[10] was dissolved in four cubic centimetres of sodium cyanide. Two lots of the solution were then treated with (*a*) reagent number 7 (molybdenum-free), (*b*) reagent number 7*b* (containing added sodium molybdate). Each was compared with five cubic centimetres of diluted uric acid standard solution, treated with the corresponding arsenophosphotungstic acid reagent, and the results were expressed as milligrammes of uric acid per hundred cubic centimetres of blood, as shown in Table X.

Thus, when molybdenum impurity is present in the arsenophosphotungstic reagent, blue colour is developed as the result of interaction with the residue left after extracting the material precipitated by silver lactate with 10% sodium chloride in one-tenth normal hydrochloric acid.

With either the Folin or Benedict methods of direct determination of uric acid, therefore, with an arsenophosphotungstic acid reagent containing molybdenum, grossly inaccurate uric acid values may be obtained.

Five cubic centimetres of protein-free blood filtrate were treated with silver lactate, the precipitate was extracted with 10% sodium chloride in one-tenth normal hydrochloric acid, and the residue was extracted with two further volumes of the same solution. The residue was then dissolved in sodium cyanide and diluted with water.

TABLE X.

Specimen. Number.	Protein Precipitant.	Uric Acid Value. Milligrammes per 100 cubic centimetres of Blood.		Thioneine expressed as Uric Acid from five cubic centimetres of Protein-free Filtrate.	
		Molybdenum-free Reagent.	Molybdenum-containing Reagent.	Molybdenum-containing Reagent.	Molybdenum-free Reagent.
1	(*a*) Molybdate-sulphuric acid.	3·1	4·7	2·3	
	(*b*) Tungstate-sulphuric acid.	3·1	4·8	2·6	
2	(*a*) Molybdate-sulphuric acid.	3·2	4·4	2·2	Very faint blue.
	(*b*) Tungstate-sulphuric acid.	3·8	4·5	2·5	Very faint blue.
3	(*a*) Molybdate-sulphuric acid.	3·6	4·0	1·8	Trace colour.
	(*b*) Tungstate-sulphuric acid (molybdenum).	3·2	4·7	2·3	Trace colour.
	(*c*) Tungstate-sulphuric acid (no molybdenum).	3·1	4·5	2·2	Trace colour
4	(*a*) Molybdate-sulphuric acid.	4·4	4·0	1·0	Faint blue.
	(*b*) Tungstate-sulphuric acid (molybdenum).	3·4	4·4	1·6	Faint blue.
	(*c*) Tungstate-sulphuric acid (no molybdenum).	4·0	4·1	1·6	Faint blue.
5	(*a*) Molybdate-sulphuric acid.	2·2	3·9	0·8	Trace colour.
	(*b*) Tungstate-sulphuric acid.	2·5	4·0	0·7	Trace colour.

A comparison was made by using residues obtained in this way with the various possible colour-developing reagents. The reagents used and the results obtained are tabulated in Table XI.

TABLE XI.

	Reagent used for Colour Development with Residues from Protein-free Blood Filtrate after Precipitation with Silver Lactate and Treatment with 10% Sodium Chloride in one-tenth normal Hydrochloric Acid, dissolved in Sodium Cyanide.	Resultant Colour.
1	Sodium molybdate + phosphoric acid.	No colour.
2	Sodium tungstate (No. 7) + sodium molybdate.	No colour.
3	Sodium tungstate (No. 7) + phosphoric acid.	No colour.
4	Sodium tungstate (No. 7) + arsenic acid + phosphoric acid. (Molybdenum-free arsenophosphotungstic reagent.)	Very faint blue colour.
5	Constituents of No. 4 boiled with sodium molybdate. (Molybdenum-containing arsenophosphotungstic reagent.)	Definite blue colour.
6	Original sample of Merck's sodium tungstate in arsenophosphotungstic acid reagent.	Deep blue colour.

From these results it seems certain that a compound consisting of phosphoric acid, molybdenum and sodium tungstate is produced during the boiling necessary in the production of the arsenophosphotungstic acid reagent. This compound reacts with some substance or substances, other than uric acid, present in the protein-free filtrate giving a blue colour. One such substance is thioneine.

Cysteine was examined with various arsenophosphotungstic acid reagents, and a blue colour

developed only when there was molybdenum impurity in the reagent. Guanosine and caffeine hydrochlorate yielded a blue colour with molybdenum-containing arsenophosphotungstic acid reagents, and remained colourless when treated with molybdenum-free reagents.

Several specimens of allantoin were also tested with molybdenum-free arsenophosphotungstic acid reagent and molybdenum-containing reagent. In one case no colour developed with the molybdenum-free reagent, whilst a deep blue colour resulted when the molybdenum-containing reagent was used. With the remaining specimens of allantoin (Merck's and British Drug Houses) a colour developed with both reagents, that with the molybdenum-containing reagent being purplish blue and more intense. These specimens were shown to contain uric acid by titrating with potassium permanganate in the presence of sulphuric acid. There was apparently sufficient uric acid present in these samples to produce blue colour, even with the molybdenum-free reagent.

In reviewing the literature it is interesting to note the criticism of Benedict[11] on the work of Bulmer, Eagles and Hunter[12] on the discrepancy between the "direct" and "indirect" methods of uric acid determination on animal blood. In connexion with their work on nickel rash, he allows that in estimating uric acid in this relatively rare condition there may be discrepancy between the two methods. He further states that:

> Even accepting that in nickel rash the direct method yields results too high, it would seem a question in the present writer's mind, as to whether such a finding should offset the fact that in hundreds of routine analyses by the direct method only a few scattered cases occur where there is significant difference in the two methods.

A close examination of the series of figures given by Bulmer, Eagles and Hunter[12] reveals the fact that six out of the fourteen subjects were normal, healthy men, yet these had uric acid values of the same order of magnitude as those for the nickel rash patients for both methods. In view of my own experience with molybdenum-containing sodium tungstate, it seems likely that the explanation of the results of Bulmer, Eagles and Hunter lies in the fact that they were using molybdenum-containing sodium tungstate in their arsenophosphotungstic acid reagent, whilst Benedict was fortunate in obtaining a pure sodium tungstate for his reagent.

From the results of this investigation it seemed advisable to perform a further series of uric acid determinations in the blood of toxæmic pregnant women, normal pregnant women, and non-pregnant women, using an arsenophosphotungstic reagent free from molybdenum impurity. The results are tabulated in Table XII and indicate a tendency for eclampsia to be characterized by high uric acid values, the average figure being higher than the generally accepted normal upper limit of 3·5 milligrammes. In the normal pregnant group 80% of the values fall below 3·5 milligrammes per 100 cubic centimetres of blood, and are in agreement with the accepted values.

TABLE XII.

Condition.	Number of Cases.	Maximum.	Minimum.	Average.
Normal (pregnant) ..	18	5·2	1·7	2·8
Pyelitis	14	5·9	2·1	2·8
Slight albuminuria ..	11	3·6	1·6	2·5
Albuminuria	21	8·3	1·9	2·9
Hyperemesis	2	2·5	2·0	2·2
Nephritis	12	6·0	2·1	3·0
Pre-eclampsia	8	4·6	2·6	3·5
Eclampsia	6	6·7	2·7	4·9
Non-pregnant—Surgical	17	4·6	1·7	2·6
Non-pregnant—Surgical, with chronic nephritis	3	2·5	4·8	3·8

Summary.

The Benedict, Folin and Wu, and Morris and Macleod direct methods for determining uric acid are compared. Lower values were consistently obtained with the Morris and Macleod method.

The purity of the various reagents used was tested. Arsenophosphotungstic reagents prepared with molybdenum-containing sodium tungstates gave a purplish-blue colour, and uric acid values were definitely higher when such reagents were used.

Thioneine (and other substances) in the blood filtrate react with molybdenum-containing arsenophosphotungstic acid reagent, giving a purplish-blue colour and a high uric acid value.

The molybdenum impurity in the arsenophosphotungstic acid reagent is the important factor in producing the high uric acid values when thioneine is present in the blood filtrate, rather than this impurity in the sodium tungstate used in precipitating the protein being responsible for the presence of the thioneine in the protein-free filtrate.

A method for preparing molybdenum-free tungstic acid from impure sodium tungstate and the preparation of an arsenophosphotungstic acid reagent from this tungstic acid are described.

The purplish-blue colour is shown to be due to interaction between a compound formed from molybdenum, phosphoric acid and sodium tungstate during the boiling necessary to prepare the arsenophosphotungstic acid reagent, and thioneine (and possibly other substances) in the protein-free filtrate. Cysteine, guanosine, allantoin and caffeine are capable of producing this colour.

Conclusions.

If molybdenum-free sodium tungstate is used in the preparation of the arsenophosphotungstic acid reagent for the Benedict direct method of estimating uric acid, the method is capable of giving accurate results.

If, however, molybdenum impurity is present in the reagent, grossly inaccurate values result, owing to the interaction with thioneine and other substances in the protein-free filtrate.

The average value for uric acid in normal pregnant women is 3·5 milligrammes per 100 cubic centimetres of blood.

In eclampsia there is a definite tendency towards higher values.

Higher values may also occur occasionally in other toxæmias, although the average values in all cases lie below 3·8 milligrammes per 100 cubic centimetres of blood.

Acknowledgements.

I wish to thank Miss Joan Norris for the work done at the Dunn Laboratory, Saint Thomas's Hospital, London, on the comparison of the chemicals used in the biochemical laboratory at the Melbourne University with those used at the Dunn Laboratory.

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THE DEVELOPMENT OF A TECHNIQUE IN TREATMENT OF CANCER OF THE CERVIX UTERI.[1]

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AND

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THESE remarks are based on a consideration of ninety-six patients with carcinoma of the *cervix uteri* treated at the Perth Hospital since its inception as a radiotherapeutic centre in March, 1929.

All of these patients had radiation therapy in some form, and various combinations of methods of treatment, different filters and forms of radium, different doses *et cetera* have been tried. Patients treated by operation alone are not included, but it is found that there are no records of a hysterectomy performed primarily for cancer of the cervix within the last two years.

At present, while no strict method has been adopted for any particular case, the general procedure has been developed and varies only where the type of growth demands. Mainly, both X rays and radium are used in conjunction.

[1] Read at the Fourth Australian Cancer Conference, Canberra, March, 1933.

The steps in treatment are as follows: The patient is admitted to hospital and kept in bed for two days, during which the aim is to achieve cleanliness of the vagina. If considered necessary, cystoscopic examination is carried out.

Spinal anæsthesia is found to be satisfactory. Only low anæsthesia is necessary, and while relaxation is perfect, no after-effects have been noted.

The cervical canal is dilated and a uterine pack is passed into the uterus. It consists of tubes of radium, from 40 to 45 milligrammes, complete active length four centimetres, filtration of one millimetre of platinum equivalent and three millimetres of rubber. The radium is bound in the rubber covering, the tubes lying in tandem. The whole pack is, if possible, sutured near the external os. This has been found necessary to be sure that the pack stays in the uterus.

A vaginal dose is administered by the use of two, three, or four colpostats. The colpostats are ordinary corks, two centimetres in diameter by three centimetres long, which contain a ten-milligramme radium tube (filter one millimetre of platinum equivalent, one centimetre active length) forced into the centre. They can be roughly shaped to meet any local needs. They are placed one in each fornix and between, according to the capacity of the vagina.

Packing of the corks in position is carried out with gauze so that the rectal and vesical walls are held as far away as possible. A rubber catheter is laid along the posterior vaginal wall up to the cervix. The vagina is well packed and the introitus is sutured over the pack.

The colpostats in certain cases are supplemented by the use of interstitial needling, should such be thought necessary; for example, for extension of the tumour along the anterior vaginal wall.

After-treatment consists merely in the instillation of a few ounces of flavine or mercurochrome through the catheter twice daily. The pack is thereby saturated from above and can be kept in position for long periods without discomfort.

The length of treatment varies, but an average dose of 8,000 milligramme-hours (120 hours) is applied. A dose up to 12,000 milligramme-hours has been given without injurious local effect. The time of in-patient treatment averages twelve days.

Some complications have been noted:

1. Sepsis. Although all types and conditions of tumour have been treated, signs of infection have been limited. In about 30% of cases a rise of temperature has been noted up to, but rarely over, 37·8° C. (100° F.), which occurs after the first few days. In only one case has severe infection occurred. It was probable in this case that, during introduction of the radium, the peritoneum was opened.

2. Proctitis. Five patients have needed treatment for proctitis, as indicated by symptoms of tenesmus and diarrhœa. In all but two it yielded to simple treatment in under one month. In both others the posterior fornix was infiltrated. One of these

patients is at present dying with a large mass in the anterior rectal wall. The other has a stricture two inches from the anus, which is believed to be malignant. None of these patients, except the last, was examined by proctoscopy; and in the last-mentioned patient no affection of the mucous membrane was noted.

3. Cystitis. No patient complained of urinary symptoms, although in some cases needles were used in the anterior vaginal wall.

4. Post-radiational hæmorrhage has occurred in two cases. One responded to treatment. One patient died from a sudden severe hæmorrhage occurring the day after removal of the radium. The condition was very advanced.

5. As a complication may be mentioned the formation of adhesions about the upper vagina. Although patients are instructed in regard to douching until the reaction is healed, the eroded vaginal walls occasionally form adhesions which, if allowed to persist, result in the conversion of the cervical region into a small abscess cavity. The retention of pus prevents the clean healing of the vault. On this account patients are examined at the end of the month from the beginning of treatment.

Naturally, all patients submitted cannot be treated along the above lines. For example, of twenty consecutive patients recently treated, seventeen were treated as above; in three of these cases needles were used as well. Two patients received X rays only, owing to the late stage of the disease. In one case an extensive pyometra was opened when the cervix was being dilated, so that radium was abandoned. The use of X rays resulted in sufficient healing to render radium application possible at a later date.

Following the radium it is aimed to give the patient a course of X rays to the pelvis within the first few weeks. The dose is made to give a distinct erythema to the skin—near the limit of safe tolerance for routine use. Two ports, anterior and posterior, from the pelvic brim to the pubes, and unlimited laterally, are used at factors of 200 kilovolts and a filter of one millimetre of copper *plus* one millimetre of aluminium. The whole is given in four or six sessions within two weeks. A mild proctitis may follow this treatment.

No symptoms referable to radiation cystitis have been noted, a result contrary to what should be expected if the bladder mucosa were as sensitive as has been suggested by various authors.

In a few cases, while the patient was waiting for radium treatment, a course of X rays had been instituted on the patient's admission to hospital. Certain advantages are claimed for such a routine, but possible injury to the bowel and bladder are more difficult to control. Patients are examined every month for the first half year. A second course of X rays is sometimes given at the end of this period at similar factors to those recorded above.

TABLE I.

Period of Observation.	Total Number.	Stage. I.	Stage. II.	Stage. III.	Stage. IV.	Operability.	Types of Application.	Average Dose.	Alive and Well.	Alive with Signs.	Dead.	No Record.	Total.
						%		Milligramme Hours.					
More than three years..	15	2	1	10	2	20	A. Intrauterine tube of 20 milligrammes (1 millimetre platinum). B. Interstitial tubes of 5 milligrammes (0·5 millimetre platinum).	4,000	4	2	9	0	15
Over two and less than three years ..	29	9	2	16	2	34·5	A. Interstitial treatment with (i) needles 0·5 millimetre platinum, (ii) tubes 5 milligrammes 0·5 millimetre platinum. Various combinations of these.	4,100	12	4	4	6	26
							B. Treated by X rays only. (Two cases were prophylactic after hysterectomy.)		2	0	1	0	3
Over one year and less than two years ..	29	4	7	14	4	38	A. Radium tubes and needles as above, in various arrangements.	4,270	7	2	2	1	12
							B. Radium tubes and needles together with X rays.	4,900	3	1	0	0	4
							C. X rays only.		0	1	3	1	5
							D. Regaud method with X rays.	9,600	3	3	1	1	8
Treated within last year	23	7	2	7	7	40	A. Tubes and needles as above.	4,240	3	0	1	0	4
							B. X rays only.		1	1	0	0	3
							C. Regaud method with X rays.	6,300	11	4	1	0	16
Total	96	22	12	47	15				46 48%	18 19%	23 24%	9 9%	

After six months they report every three months for examination.

As stated above, this is the routine method used at Perth at present, as developed over the last year and a half. Earlier methods have been tried. Previously, interstitial needling with needles of 0·5 millimetre of platinum equivalent filter were tried. Still earlier, five milligramme tubes, with a filter of 0·5 millimetre of platinum equivalent, were inserted into the growth. In some cases X rays only have been used, and in others X rays have been combined with radium. The results are recorded in four groups, each extending over one year.

Regarding these statistical results it may be mentioned that:

1. As an indication of choice of method, the numbers are too small to give definite information. Moreover, the Regaud method, which is outlined in detail above, has a greater applicability to all types of cases, so that it is being used where formerly only X rays would have been used. The total milligramme-hour dose is stated merely as a suggestion of the dosage necessary. Naturally, needling does not require the same length of treatment as does the Regaud method, which practically amounts to distant radiation, so that the times are not comparable. As stated above, where the mass of tumour is large, the length of treatment can be increased considerably beyond that generally advocated, and thus a larger range of tissues receives adequate radiation. With care doses up to ten and eleven thousand milligramme-hours can be given without permanent damage to the surrounding structures. It is to be noted that each year the operability rate has risen, indicating possibly the change of opinion of the gynæcologists who have sent the patients to the department—those patients in early stages who would formerly have been treated by surgical operation only are now receiving radiation treatment.

2. The stage of the disease has been recorded on the classification suggested by the League of Nations. Stages I and II are considered operable.

3. Amongst this series of ninety-six cases, fourteen were found to have had a previous hysterectomy, but the type of operation was not stated.

In three of the earlier cases recurrence had occurred in the vagina when the operation had been performed for recognized malignant disease of the cervix.

In one case the presence of a neoplasm was found during operation for a condition thought to be benign.

In one case the malignancy appeared four months after operation and may have been the cause of the original symptoms. These have little significance.

Of the remaining nine cases partial or complete hysterectomy had been performed for reasons not associated with malignancy, and the cancer had subsequently developed in the stump of the cervix or upper part of the vagina.

Three cases appeared from nine to twelve months later, one at one and a half years, three about four years, and one twelve years after the operation.

The high percentage is noteworthy and recalls the suggestion that the parts left after subtotal hysterectomy are particularly susceptible to the development of malignant change. For this reason subtotal hysterectomy has been abandoned at the Perth Hospital and is replaced by the more complete operation.

In the cases recorded confirmation by biopsy has not been commonly performed.

In the earlier groups the selection of cases for radiation by radium was stricter than at present. The technique outlined above has been found to have more general application and has been adopted on the grounds of simplicity and reliability of results from a consensus of opinion by different workers.

In conclusion, the work has been carried out under the direction of the staff of the hospital, and is an expression of the general opinion that better results are being obtained by radiological than by surgical measures.

Reports of Cases.

LEPROMA OF THE CORNEA.

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IN view of the recent discussion upon leprosy and the few cases among white people reported in Australia, it might be advisable to report the following case.

The Ophthalmic Condition.

(By Clifford Colvin.)

On October 7, 1930, Mrs. M., aged 82 years, called to see me, complaining of soreness of both eyes. As she walked in, supported by her husband, I was struck by her peculiar gait, obviously due to foot-drop. She had double facial paralysis, marked ectropion of both lower lids, and lagophthalmos of both eyes, with resulting mild chronic conjunctivitis. Vision in the right eye with correction, was $^{6}/_{36}$; with the left eye she could appreciate hand movements only.

There was keratitis of the right cornea due to lagophthalmos. There was a calcareous type of degeneration, with slight thickening and scarring just inferior to the centre of the cornea.

In her left eye there was a large granuloma-like mass projecting from the cornea in its lower two-thirds, and extending down just over the limbal margin. It was about ten millimetres in diameter, and about eight millimetres in height, and of a dark yellowish colour, with a tendency to dryness and scaliness at the apex.

Ciliary injection was present in both eyes. Both pupils were active to light and accommodation. The external ocular muscles were normal.

Owing to the protrusion of the mass it was decided to remove it, which was done by cutting through the base as close to the corneal surface as possible. The growth was sent to Dr. Dawes for examination.

The cornea healed well and the patient was free of pain in her eyes. Her vision, needless to say, was not improved. Suspecting leprosy from the general condition of the patient, I asked Dr. Paton to see her. His report and that of Dr. Dawes are appended.

The interesting points in this case are that the condition had been present for 35 years.

She was born in New South Wales and had always lived in the west, and had not been out of the State. Her husband had attended her during that time and showed no symptoms of the disease, and, though she had seen numerous medical men, and had been in hospital in Sydney, her condition had apparently not been diagnosed.

The Physical Examination.

(By Dr. J. T. Paton.)

Dr. Colvin asked me to see this patient on October 7, 1930. She was tall, pale and heavy, quite exceptionally well covered with adipose tissue for her age. Her lower lids were everted and her cornea dim. She had sought Dr. Colvin's advice about her sight, and had no complaints about her general health, so that a history had to be elicited by cross-questioning.

The first thing I noticed was the peculiar condition of her hands and fingers. The terminal phalanges of most of her fingers had almost disappeared, and the nails in several were projecting from the centre of the base of the phalanx like a bird's claw. When asked how she had lost her phalanges, she said that in 1896 she had lost sensation in the little finger of her left hand, and that gradually whitlows had developed on her fingers but that they were painless. Some of the phalanges had been amputated and some had just been slowly absorbed. Later she had noticed that the sensation in her legs was going, and she developed drop-foot, and had difficulty in walking; otherwise her health was excellent.

An examination revealed complete loss of all forms of sensation from the elbows to the fingers, and from the knees to the toes; sensation was normal elsewhere. Some thickening of the ulnar nerves appeared to be present, but I was not quite sure of this. There was some wrist-drop; the hands were held in pronation; full supination was not possible. She could approximate her thumb to her little finger, and flex and extend her fingers; wrist extension was imperfect. She had foot-drop, some wasting of the calf muscles and peronei, and inability to extend or evert at the ankle joint. Her knee jerks were present, and the plantar response was flexor. Double facial paralysis was present.

I thought her symptoms at first to be suggestive of syringomyelia; but the distribution of the sensory loss and the complete absence of sensation were against that, so I made a tentative diagnosis of anæsthetic leprosy in fear and trembling, as I had never seen a case since I was a student. Dr. Dawes was able to confirm this by finding leprosy bacilli in the corneal granuloma, and, later, Dr. McMaster, of the Coast Hospital, agreed that it was so.

She has been looked after most carefully by her husband ever since the illness started, thirty-five years ago, and apparently he has not been infected.

Pathological Report.

(By Dr. S. R. Dawes.)

I was asked by Dr. Paton to examine a nasal swab for leprosy bacilli; but in three swabs, two being taken after leprosy bacilli had been found in tissue removed from the eye, no leprosy bacilli were seen.

The piece of tissue removed from the patient's eye was given to me by Dr. Colvin. It was about four to six millimetres in diameter. Sections showed granulation tissue of a somewhat cellular nature. Round cells resembling non-granular leucocytes were seen against a background of connective tissue, in which there was no marked fibrosis. The tissue was uniform in appearance; there was no tendency to focal arrangement. There was no evidence of necrosis. Giant cells were not seen. Sections were stained with carbol-fuchsin, and acid-fast bacilli were demonstrated in large numbers. So numerous were they that a slide counter-stained with methylene blue showed a reddish colour through the blue. These bacilli, which conformed to the appearance of leprosy bacilli, were crowded in large numbers in the round cells. The character of the granulation tissue, together with the appearance and staining properties of the bacilli, are sufficient for the conclusion that the condition is due to the leprosy bacillus.

Reviews.

A HANDBOOK OF PRACTICAL ANATOMY.

"PRACTICAL ANATOMY", by Six Teachers, is a practical anatomy manual in one volume. It is the result of the individual work and collaboration of six eminent British anatomists.[1]

Professor W. Wright has dealt with the abdomen and pelvis; Professor T. Yeates has dealt with the thorax; Professor J. S. B. Stopford is responsible for the section on the central nervous system; Professor S. E. Whitnall has written on the orbit, eye and ear; Professor Mary F. Lucas Keene has dealt with the head and neck, and Professor E. B. Stibbe with the limbs. The whole work has been edited by Professor Stibbe.

This book is intended to replace the "Practical Anatomy" of Parsons and Wright, much of whose material, both in text and illustration, has been freely utilised. We have nothing but praise for this excellent publication. It has cast off many time-worn shackles, and all that is new by way of arrangement, illustration and diagram is admirable. It is satisfactory to note that the central nervous system has been divorced from the head and neck and has been treated as a separate anatomical unit. In the same way the orbit, eye and ear have, we think wisely, been considered in a separate section.

As far as nomenclature is concerned, the authors have seen no sufficient reason to depart from the old terminology; they have, however, not been consistent, and have used terms from the B.N.A. nomenclature where it seemed desirable. The wisdom of this course is debatable. The number of new drawings of dissections, mainly the work of Miss W. M. Barclay Smith, are most praiseworthy and are one of the most striking features of the book.

PROGRESS IN RADIOLOGY.

IT is impossible for a radiologist to read all the various journals published throughout the world, many of them in foreign languages. Dr. Waters and Dr. Kaplan have compiled the "Year Book of Radiology", which is actually a large collection of abstracts from the literature published during 1932.[2] The book consists of two parts, the first dealing with radiological diagnosis and the second part with radiotherapeutics. If it could have been arranged so that the illustrations came on the same pages as the articles to which they belonged, the book would have been easier to read. However, this book is a veritable mine of information and gives a comprehensive outline of all the latest work that has been done in every branch of radiology. The book will not only be greatly appreciated by X ray specialists, but will be found almost invaluable to all those practitioners who use X rays in connexion with their practice and who wish to keep themselves conversant with the latest developments. Much of the value of this edition will be lost if a new volume is not brought out each year, and it is hoped that the authors will once more set to work and produce a year book for 1933 on similar lines.

[1] "Practical Anatomy", by Six Teachers. Edited by E. P. Stibbe, F.R.C.S.; 1932. London: Edward Arnold and Company. Demy 8vo., pp. 731, with illustrations. Price: 30s. net.

[2] "The 1932 Year Book of Radiology": "Diagnosis". Edited by C. A. Waters, M.D.; and "Therapeutics". Edited by I. I. Kaplan, B.Sc., M.D.; 1932. Chicago: The Year Book Publishers. Royal 8vo., pp. 750, with illustrations. Price: $6.00 net.

The Medical Journal of Australia

SATURDAY, JUNE 3, 1933.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: Initials of author, surname of author, full title of article, name of journal, volume, full date (month, day and year), number of the first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction, are invited to seek the advice of the Editor.

THE HOBART CONGRESS.

MAN is largely a slave to habit, and the medical man no less than others. Some habits may be looked on as good, and others as bad; others again are so unimportant as not to need description. One of the most characteristic habits of the medical practitioner, known to himself and to many of his unfortunate friends, is that of talking shop. This habit is good when it is indulged among medical men alone; it becomes bad when it proclaims itself in the presence of non-medical people. The habit of talking shop at congresses is most useful, for there men are gathered together from distant states and countries and experiences are exchanged in a way that cannot fail to widen the outlook and increase the enthusiasm of all participants. It is for this reason that very often the informal discussions of small groups of workers gathered at a congress are more valuable than the set papers read at sectional meetings. Congresses are held so seldom that the congress habit may lose its grip. It was for this reason that satisfaction was expressed with the decision of the Federal Committee to accept the invitation of the Tasmanian Branch of the British Medical Association to hold the fourth session of the Australasian Medical Congress (British Medical Association) at Hobart in January of next year.

Since the invitation of the Tasmanian Branch was accepted, an executive committee has been formed and considerable progress has been made with the preliminary arrangements. In previous congresses executive committees have had ample time to make their plans; they have not been hampered by the constant reminder of financial depression nor on that account by the careful ministrations of enthusiastic people who specialize in the use of wet blankets. On this occasion the time available for planning the congress is all too short. The Tasmanian Executive Committee is alive to the importance of the work that it has undertaken, and every member of that committee is determined to make the congress a success. They cannot do this alone. They must have the cooperation of members of the Branches both in Australia and New Zealand. The subject has been mentioned previously in these pages and will be referred to again as time goes on.

As announced in last week's issue, Dr. D. H. E. Lines has been appointed President of the session. Those who know Dr. Lines realize that he is well qualified for the important office, in that he is a man of wide sympathies and has had a vast experience in medicine and in the activities of the British Medical Association. Dr. H. Nairn Butler and Dr. W. L. Crowther are the Joint Honorary Secretaries, and Dr. Stuart Gibson is the Honorary Treasurer. In stating that the congress will be held at the University of Tasmania and at the Philip Smith Teaching College we take this opportunity of expressing the appreciation of the executive and of the Tasmanian and other Branches for the ready cooperation and the assurance of help in both accommodation and equipment given by the Chancellor of the University and the Director of Education of Tasmania. The point which more than any other needs to be emphasized is that all the work of the Executive Committee and of the other office-bearers, all the offers of help (and they are many) from outside the medical profession will be nullified unless medical practitioners realize that early enrolment of members of congress is essential. Application for membership must be made at once.

Hobart is a popular tourist resort in the summer, and normally the accommodation for visitors is heavily taxed. Unless application for membership is made at once, members may find it impossible to secure accommodation. It has therefore been suggested that, on enrolment, members should communicate with Dr. E. A. Rogers, of Macquarie Street, Hobart. Dr. Rogers is Secretary of the Transport and Accommodation Committee. He will be able to furnish all necessary information about hotel and boarding house accommodation, about shipping arrangements, transport of motor cars by sea and so forth. Dr. Rogers will also be prepared to book accommodation and to arrange for steamer passages. In this connexion it should be noted that Huddart Parker, Limited, and the Peninsular and Oriental Steam Navigation Company, Limited, have been most helpful in arranging dates of the sailings of their ships so that they may be available for members of congress. Arrangements have been practically concluded for one of the larger Huddart Parker steamers to take passengers from Sydney to Hobart, to accommodate them during the congress and to bring them back to Sydney. A P. and O. mail steamer will take passengers to Hobart from Brisbane and Sydney, and another will carry passengers to Hobart from Fremantle, Adelaide and Melbourne.

In our previous announcement of the congress it was suggested that medical practitioners should make the congress the occasion of a holiday. The island of Tasmania is second to no place in Australia for holiday and tourist facilities. At a later date a special article dealing with this aspect will be published. At present the message to members of the Branches is to enrol at once and to secure accommodation through Dr. Rogers without delay.

Current Comment.

LETHARGY.

IT is natural that fatigue should have interested all scientists concerned with animal activities; and the experimental physiologist has illuminated the subject from several aspects. As a clinical phenomenon it is no less interesting, and all those engaged in the practice of medicine are familiar with a lessened capacity for withstanding exertion as a symptom of very many morbid processes. For example, the readiness with which fatigue may be produced in an early but toxic stage of a systemic disease like pulmonary tuberculosis is often very notable, and what is even more interesting is the familiar fact that the objective and subjective signs of that toxæmia are almost identical with those of bodily fatigue. But, setting aside the undue readiness to feel fatigue of those suffering from recognizable disease, it is a matter of common experience that there are individuals whose capacity for withstanding mental and physical exertion is distinctly limited, even though they are apparently otherwise in good health. Does this depend upon some biophysical or biochemical idiosyncrasy, some maladjustment of endocrines, some defective neuromuscular endowment? Even if we invoke the aid of the mystic word "diathesis" we must admit that surely there is some underlying physical basis for this peculiarity. Louis Berman has gone so far as to recognize a definite clinical syndrome of "fatigability", whose common symptoms are a "lessening of vitality", with a well marked neuromuscular asthenia, loss of attention and concentration, forgetfulness and even depression and melancholia.[1] In 1929 he wrote on this same subject, but now he attempts to correlate this state with a chemical anomaly. He reported twelve cases originally, and now adds thirty-two others, and in these later cases has investigated the blood chemistry. This, he claims, reveals a much lowered blood cholesterol, which may be raised to a normal level by the use of irradiated lanolin, and to the syndrome he gives the imposing name of "asthenia cholesterolpriva". All his patients showed in varying degree the symptoms enunciated above, and the muscular asthenia was very definite. In some cases atrophy and even pseudo-hypertrophy of the muscles was noted, suggesting a muscular dystrophy. But usually the muscles, though fatigued with extreme readiness, showed no atrophic change, though they were flabby and toneless. No myotatic irritability was noted, nor myoidema, though twitchings sometimes occurred. The electrical reactions were normal. No muscular subjective sensation was complained of by the patients. An interesting feature was the occurrence of an increased pigmentation in some instances, and obviously this suggests endocrine disturbance. The blood sugar was sometimes found to be below normal level, as was also the inorganic phosphorus; otherwise the only abnormality was the low blood cholesterol. This averaged 85 milligrammes per 100 cubic centimetres in the 32 cases, and was never higher than 115 milligrammes. Moreover, the lower the cholesterol, the greater the degree of fatigability of the patient. Berman remarks that a low blood cholesterol has been observed also in malnutrition, pernicious anæmia, Addison's disease, hyperthyreoidism, and muscular dystrophies, and

[1] *Medical Journal and Record*, February 15, 1933.

he looked carefully for signs of such morbid states in his patients. Turning to the therapeutic side, he failed to raise the level of the cholesterol in the blood by feeding, and thus tried inunction. The patient was given a hot bath, lanolin was rubbed into the skin of the chest, abdomen and thighs until it glistened. After fifteen minutes ultra-violet light was applied, the application starting with a three-minute dose and increasing to ten minutes on each alternate day. He also used irradiated lanolin with equally good results. A rise was found to occur in the blood cholesterol of all the patients, and the treatment was continued till the normal level was reached. This occurred in about three months, and it was not found possible thus to cause hypercholesterolæmia either in these or in normal persons. Recurrences did not occur up to the time of the report. Ultra-violet light alone caused no rise in the cholesterol of the blood.

Obviously, this work should be repeated and critically examined. Whether a "new" syndrome has been discovered or not is not certain. The author reports that one patient suffering from ovarian dysfunction and with hypocholesterolæmia did not benefit from treatment. But this serves as a reminder that endocrine dysfunction, except in certain of the clear-cut and well-recognized types, is still a vague thing, and we must be cautious. The most important aspect of the whole report is the claim that the patients were relieved of their symptoms. If such people can so simply be rendered more capable of withstanding fatigue, this is a very useful observation. But a certain degree of scepticism is perhaps pardonable, for whereas the amount of cholesterol in the blood can be exactly measured, there is a definitely psychological side to the outputting of mental and physical energy. That there must be some coordination between a measurable blood state and a patient's clinical condition may be admitted; for example, the sedimentation rate has been found to parallel the physical state in certain diseases. It would therefore be interesting to see the results of further confirmatory work on the subject.

LEGALIZED ABORTION IN RUSSIA.

IN view of the interest that has centred round the reports of legalized abortion in Russia and because of the difficulty of obtaining reliable information about anything that occurs in that distressful country, it is appropriate to draw attention to a recent summary of the medical sequelæ of legalized abortion as practised in Russia. These sequelæ were reported at a congress in the Ukraine and have been summarized by A. Mayer.[1] Mayer states that the patients were operated upon at special centres by experts working under good conditions. The results do not support the opinion frequently expressed or assumed that such operations are free from complications. Perforation of the uterus was uncommon and a conservative policy was adopted with success in all cases unless hæmorrhage or prolapse of viscera occurred. The immediate mortality after abortion was not high (0·7%), but, as Mayer points out, this figure was greater than the general maternal mortality and was mainly due to interference in women already infected from previous abortions or by gonorrhœa. Mild pyrexia in the puerperium was very common, although severer grades were rare. In this connexion it must be remembered that most patients left hospital on the third day and any later developments were not recorded in the case notes. However, some of the statistics showed the effect of repeated abortions in producing either generalized or localized pelvic infection. Because of the production of abortion on such a large scale, many late effects not hitherto observed in other countries have become important. As a result of the vigorous use of the curette scarring of the cervix and uterine wall were common, with consequent amenorrhœa or oligomenorrhœa. Cystic degeneration of the ovaries was also observed in many instances of sterility. The biological trauma induced by the sudden interruption of the connexion between the growing ovum and the maternal tissues tended to produce two distinct types of endocrine disturbance. In some cases there was a condition resembling a pituitary dystrophy with excessive fat deposits, and in others genital atrophy and hypoplasia were noted. Parametritis and perimetritis with tubal involvement occurred in 25% of the cases as an early complication and to a much greater extent as a late manifestation of infection. Very few patients had more than three or four induced abortions because by that time they were sterile. The incidence of ectopic pregnancy was greatly increased according to all observers. The effect on future pregnancies and labours showed clearly the rôle played by abortion in causing latent infection. The incidence of fever during labour and infection of the *liquor amnii* exceeded three times the normal rate. The duration of labour was more than doubled and abnormal adhesions of the placenta were seven to eight times as frequent, leading to a marked increase in *post partum* hæmorrhage and manual removal of the placenta. The natal and neonatal death rate was high, owing to the prolongation of labour and the degenerative changes in the placenta. A great increase in psychic symptoms following abortion was observed—hysteria, depression, frigidity and dyspareunia. Many of the speakers at the Russian congress were alarmed because the birth rate was seriously affected, since the majority of women were between twenty and thirty years of age and so many had become sterile before they bore a living child. Finally, it was admitted that legalizing abortion had not stamped out criminal abortion as was hoped when the law was promulgated. Mayer ends his survey with an earnest plea to the German profession to take heed of these unexpected results before advocating similar measures in Germany.

[1] *Zentralblatt für Gynäkologie*, November 12, 1932.

Abstracts from Current Medical Literature.

THERAPEUTICS.

Hypertension.

L. DAUTREBANDE (*La Presse Médicale*, February 15, 1933) discusses the treatment of experimental chronic hypertension. The depressor nerve of Cyon-Ludwig and the sinus nerve of Hering arise in the neighbourhood of the origin of the aorta and of the carotid sinuses respectively. Section of these nerves on both sides causes hypertension and persistent tachycardia in dogs and rabbits; these nerves, therefore, have normally a depressor tonus. The nerves were divided in three dogs, and the arterial pressure was noted once a week. While the dogs were healthy, variations in blood pressure were observed from week to week, but this pressure did not vary during observations lasting for five minutes at a time. When the dogs were ill, variations in pressure occurred, lasting for ten to twenty seconds only. These rapid variations indicated a serious impairment of the general health. Administration of papaverine, trinitrine and sodium nitrite at different times had no effect whatever on the arterial pressure of the animals. Amyl nitrite, however, produced a fall of arterial pressure on injection or inhalation through the trachea; but when inhaled through the nose it caused a definite rise of pressure, similar to that produced by irritation of the nasal fibres of the trigeminal nerve. It is suggested that amyl nitrite should benefit angina in patients without hypertension; and that hypertension in the coronary arteries, which have no vasomotor nerves, is the probable cause of temporary improvement in the myocardial circulation. Benzol, which on inhalation causes a fall of arterial pressure in animals, has no such effect when given by mouth.

The Occurrence of Active Œstrogenous Substances in Bitumen.

S. ASCHHEIM AND W. HOHLWEG (*Deutsche Medizinische Wochenschrift*, January 6, 1933) find that œstrogenous substances were present in bituminous substances (petroleum, peat and coal) of the biological character of folliculin hormone. The amount present varies with the material. Brown coal contains 400 mouse units per kilogram; coal contains 1,000; petroleum, 1,000 to 2,000; asphalt, 10,000; and peat, 500 units. The authors assume that these substances originate from the precursors of bitumen, namely, animal and vegetable remains.

Glycocoll Treatment of Progressive Muscular Atrophy.

S. KOSTOKOW AND A. SLAUCK (*Deutsche Medizinische Wochenschrift*, February 3, 1933) have investigated seven patients with progressive muscular atrophy and four normal patients during glycocoll therapy (five grammes three times a day) and come to the following conclusions: (i) Glycocoll plays a certain part in the physiology of muscle. Apart from its main function being creatin formation, no other function is known. (ii) In cases of muscular dystrophy, there is an inability to use creatin within the body. Glycocoll treatment restores this function. (iii) As a result of treatment, patients complained of a sensation of pins and needles, tension and tearing feelings in the muscles, marked twitchings and movements in the regenerating muscles, and a diminution of weakness and an increased function. As long as there is some muscle tissue present, the power increases, and this is recorded on the tensionmeter. In addition, there is a decrease in the size of the affected muscles. Some people learnt to walk again and could do their work, whilst two lost their thirst and needed less fluid. From these results the authors conclude that glycocoll has produced far better results than was anticipated.

The Physiological and Pharmacological Effects of Cholin.

K. SCHÜBEL (*Münchener Medizinische Wochenschrift*, February 3, 1933) writes that acetylcholine is widely distributed in the human and the animal body and must therefore be produced in the body. It is considered to be a parasympathetic hormone. It is well protected against chemical changes in the body, for it is easily altered when it comes into contact with alkali or the esterase of the blood. Cholin is not free in the circulation and its origin is still unknown. It has a paralytic effect on the ends of the motor nerves and a stimulating effect on the ends of the parasympathetic nervous system. The administration of acetylcholine has produced a favourable effect in certain illnesses, especially in hypertension, eclampsia, and in diminished glandular and bowel function.

Treatment of Joint Disease with "Sanocrysin".

KNUD SECHER (*Deutsche Medizinische Wochenschrift*, January 20, 1933) states that "Sanocrysin" has been used in the treatment of rheumatic joint disease. The same reactions as are seen in tuberculosis treatment occur (rise of temperature, erythema, albuminuria). Pain and swelling of the affected joints are noted. The commencing dose was 0·25 gramme, and this was increased to 0·75 gramme. The more widespread the disease, the more careful must one be with the dose, for often severe skin reactions occur. Till now, the treatment in cases of chronic progressive arthritis has been unsuccessful, whilst in the progressive polyarthritis a better response occurs. Seven patients with *febris rheumatica* and *polyarthritis acuta* who failed to respond to salicylate therapy were discharged fit and well after "Sanocrysin" therapy. The therapeutic results of this therapy usually appear within a few days.

Insulin in Malnutrition.

R. D. METZ (*Annals of Internal Medicine*, December, 1932) discusses the literature on the subject of the treatment of non-diabetic malnutrition by means of insulin injections, and reports personal observations. Malnutrition of all kinds not associated with serious organic disease can be treated in this way. Patients with good appetite respond best. When anorexia is marked, larger doses of insulin are required. Injections of five or ten units are given twenty minutes before the midday meal. Up to twenty units can be given at one dose if tolerance is good. The patient is advised to eat more than the usual amount of food. Once initiated, the patient can give the injection himself. Clerical workers responded better than manual labourers. Hypoglycæmia, about two hours after injection, is to be guarded against by ingestion of sugar or barley sugar if symptoms of weakness occur. Patients with urticaria, asthma or hay fever should be treated with caution. Urticaria, œdema of the face, itching and gastro-intestinal distress may occur. Calcium lactate relieves these symptoms. Myocardial disease, *angina pectoris* and aortic disease are contraindications. Gains in weight of 4·5 to 9·0 kilograms (ten to twenty pounds) in four to eight weeks have been noted in patients with chronic arthritis, nervous dyspepsia, and debility of uncertain cause.

Epilepsy.

F. MCLAUGHLIN (*The Practitioner*, December, 1932) discusses the modern treatment of epilepsy. If full investigation reveals no serious aggravating factor, attention should be directed to correcting faulty posture, constipation, focal sepsis, insufficient rest and sleep, lack of proper work or exercise, over-fatigue, and breathing an oxygen-poor atmosphere. Adequate rest, in bed if necessary, is often of value in prophylaxis or treatment. A ketogenic diet, containing comparatively high fat content, or a prolonged fast sometimes reduces the number of attacks. These methods are most suited to institutional treatment, as is limitation of fluid intake recently advocated by McQuarrie. "Luminal" or "Sodium luminal" with or without bromides, is most valuable. An average dose is 0·09 gramme (one and a half grains) a day. "Luminal" should not be stopped suddenly, on account of the danger of *status epilepticus*. Headache, vertigo and drowsiness are symptoms of over-dosage. Belladonna with "Luminal" may reduce the number of psychic equivalents and improve the mental condition. "Sodium amytal", 0·18 gramme (three grains) by mouth or 0·6 gramme (ten grains) by rectum, may benefit excited post-epileptic states; it does not prevent seizures.

Status epilepticus may be treated by intramuscular injection of "Somnifen" (diethyl-diallyl-barbiturate of diethylamin). Lumbar puncture and free drainage of spinal fluid, and intravenous injection of "Sodium luminal", 0·36 gramme (six grains), are recommended. A 50% solution of magnesium sulphate by mouth cleanses the alimentary tract and reduces intracranial pressure. Lastly, 0·1 gramme of "Avertin" per kilogram body weight by enema should be tried.

NEUROLOGY AND PSYCHIATRY.

Psychosis and Brain Tumour.

LEO J. ADELSTEIN AND MARTIN G. CARTER (*The American Journal of Psychiatry*, September, 1932) draw attention to the fact that psychotic states may be symptoms of brain tumour. The reason why a psychosis is frequently overlooked as a symptom of brain tumour is that it is most often looked upon as an entity in itself rather than as a purely symptomatic manifestation of disease. The neurologist recognizes transient states of euphoria, depression, delirium or hallucination as part of the symptom-complex of certain cerebral tumours; the psychiatrist often overlooks the fact that a psychosis *per se* may develop as the result of a brain tumour. These authors claim that the incidence of brain tumour with psychotic symptoms is about 1%; that visual as well as auditory hallucinations are of localizing value only when they occur apart from the psychosis; and that, in the cases studied, mental symptoms were most marked when the lesion involved the frontal lobes and the *corpus callosum*.

Surgical Relief of Migraine.

D. G. DICKERSON (*The Journal of Nervous and Mental Disease*, January, 1933) reviews the treatment of migraine and reports in detail the histories of seven patients suffering from migraine whose headaches were successfully treated by ligation and section of the middle meningeal artery. He considers that the prodromal symptoms in migraine result from spasm of the cerebral arteries, while the headache is attributed to the reestablishment of the circulation and engorgement of the meningeal artery.

The Endocrine Glands and the Psychoses.

J. NOTKIN (*The American Journal of Psychiatry*, September, 1932) presents a detailed study of the psychiatric and laboratory investigation of eight mental patients among a population of 6,000 at the Manhattan State Hospital, who showed pronounced signs of some pathological change in the endocrine glands. The chemical examination of the blood and cerebro-spinal fluid was complete in every detail, as were the X ray examinations and determinations of the basal metabolic rates. There were three cases of schizophrenia, one of manic-depressive insanity, one of epileptic dementia, and three cases of hydrophrenia with emotional instability and hallucinatory episodes. The author considers that the relationship of psychotic states to endocrine dysfunction has been overrated. Endocrine dysfunction without psychoses is far more common. He found no correlation between the biochemical estimations of blood and cerebro-spinal fluid and the particular psychosis. He was unable to justify the stress which has sometimes been laid upon disturbances of calcium and lipin metabolism in relation to certain types of mental disorder. In fact, these investigations failed to disclose any definite organic ætiology for the psychoses; and the author goes no further than to suggest that the various physical handicaps of these patients is possibly "tied up with the dynamics of the mental trend".

The Treatment of General Paralysis by Diathermy.

NORMAN B. GRAHAM (*The Journal of Mental Science*, January, 1933) reports on the treatment by means of diathermy of twenty-four patients suffering from general paralysis. He claims to have produced a clinical remission of symptoms in 52% of cases, which is a higher percentage than that obtained by malaria or other form of pyrotherapy. These cases were unselected, and the diagnosis was made and confirmed by serological examination of both blood and cerebro-spinal fluid. Six patients died, but only one as the result of treatment. Diathermy treatment causes considerable discomfort, and patients have at times to be controlled with hyoscine. Three electrodes are used: one for the back and one each for the chest and abdomen. The temperature is elevated to 40° C. (104° F.) and kept up for about four hours. Treatment is repeated every ten days. The patient loses approximately 1·8 kilograms (four pounds) in weight with each treatment, but regains it in the interval. As with other forms of pyrotherapy, patients of the "expansive" type appear to gain the most benefit; the demented and depressed types showed little response, and congenital types remained unimproved. The author claims that risks from burns is negligible if ordinary care is observed, and that the mechanical control of the temperature eliminates the dangers of hyperpyrexia.

The Sex Factor in Puerperal Psychoses.

E. W. ANDERSON (*The Journal of Mental Science*, January, 1933) investigated factors in the sex life of patients presenting psychotic disorders associated with child-bearing, but was unable to establish any ætiological relationship between such factors as frigidity, marital discord or masturbation and the onset of insanity. Fifty puerperal psychotic women were examined with regard to the precipitating factor and compared with a similar number of cases of married women with mental states unconnected with child-bearing. No material differences were found. Neither could any clue be obtained as to prognosis or the likelihood of the later development of puerperal psychotic states. The author takes the view that morbid sexual trends play a precipitating part in any psychosis and are no more predominant in one psychosis than another.

Changes in the Cerebro-Spinal Fluid Following Treatment by Malaria.

B. REID (*The Journal of Neurology and Psychopathology*, January, 1933) has investigated the cerebro-spinal fluid findings in 230 cases of general paralysis previously treated with malaria. It was found that there was a tendency for the fluid to return to normal and that this became more marked as time went on. The fluid may become completely normal at the end of several years. This occurred in the majority of cases, but there were some patients, though continuing to show clinical improvement, whose cerebro-spinal fluid, even after many years, showed the typical paretic findings. Again, the writer found other cases in which the cerebro-spinal fluid showed marked improvement while clinically there was none. As a rule, the cell count was the first to approach normal, then the globulin, the colloidal reactions, and finally the response to the Wassermann test. It is as yet impossible to forecast the number of years necessary for the fluid findings to return to normal.

Subependymal Hæmorrhage at Birth.

CLARENCE A. PATTEN AND BERNARD J. ALPERS (*American Journal of Psychiatry*, January, 1933) contribute *post mortem* studies of thirty infants' brains, twenty-six of which showed definite evidence of subependymal hæmorrhage. The duration of labour, the previous health of the mother appeared to have no relation to the cerebral hæmorrhage. Nor did the type of presentation appear to play an important part. Some cases presented multiple petechial hæmorrhages in the region of the subependymal regions round the lateral ventricles. As a rule the cortex was not much involved, and there was no evidence of vascular disease as such. These authors consider that from the standpoint of future brain growth and development, the region of the subependymal is most vital. They claim that many of the cerebral birth conditions are due primarily to defective myelinization causing a failure of cerebral development. In the cases presented the authors found punctate and large hæmorrhages "in the subependymal region involving the matrix area, causing destruction and interference with spongioblasts which would eventually be concerned in the deposit of myelin by virtue of their development into oligodendroglia". They advance no theory as to the cause of these subependymal hæmorrhages.

British Medical Association News.

SCIENTIFIC.

A MEETING OF THE SOUTH AUSTRALIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION was held at the Anatomy Lecture Theatre, University of Adelaide, on November 24, 1933, DR. ST. J. POOLE, the President, in the chair.

Benign and Malignant Conditions of the Cervix Uteri.

DR. R. F. MATTERS read a paper entitled: "Benign and Malignant Conditions of the Cervix Uteri" (see page 669).

DR. ROLAND BEARD said he wished to thank Dr. Matters for his paper, and for the privilege of being allowed to read the paper beforehand. He appreciated the courtesy of the Branch in asking him to open the discussion. He would confine himself to debatable aspects of the paper.

First, the effect of pituitary (prolan *A*) activity on normal and abnormal epithelial growth of the cervix was a subject still in the experimental stage of the laboratory. He felt that they should be careful not to be unduly influenced by such phenomena. How were the malignancies in early infancy or extreme old age to be fitted into this hypothesis? They had seen a case of cancer of the cervix in a *nullipara* of twenty-three, and Dr. Beard had seen a cancer of the cervix in a patient of eighty-six. Approximately 10% of cervical cancers occurred in *nulliparæ*, and some authorities estimated it as 12% to 15%. How did this formidable minority develop cancer?

Secondly, the lacerations of child-birth, abortion and cervical dilatation were fertile causes of cervicitis. De Lee was quoted by Dr. Beard as advising immediate repair of all cervical lacerations at the confinement. He did not agree that this was either safe or practicable. But he did support early post-natal treatment of the cervical lesions. The cautery or diathermy was then very useful. The general practitioner did the midwifery in Australia, and, considering the conditions under which he worked, did it very well. He was most inadequately paid already for ante-natal supervision and for the confinement. If the cervix of the puerperal woman was to be his care, and it should be, then he should be adequately paid for it. The public should be educated to attend their doctors for such treatment, and the doctor should receive at least a fraction of what they paid their dentists.

Thirdly, in regard to premalignancy and malignant disease of the cervix, the paper touched on dangerous ground. Surgical zeal must be tempered with judgement. Some good might emerge from the work of Hofbauer and others, but it was not yet that Dr. Beard would advise radical surgical operation when animal laboratory opinions conflicted with, for example, the pathological opinion of Dr. Bull. He felt that a surgeon who did a total hysterectomy on other than sound grounds would have regrets. A cervical biopsy curettage should first be done. Unproven malignant disease should not have a routine total hysterectomy. A discriminate total operation was a different matter. The surgeon could not escape for long a 3% to 4% mortality. Victor Bonney emphasized this teaching, and who could be more radical than he, if the occasion demanded? Total hysterectomy was a very good operation, but a balanced interpretation of its indications was necessary. A 0·5% occurrence of cancer of the stump might be expected after carefully chosen subtotal hysterectomies, and the average post-operative life of these women would be approximately five to eight years. One must offset this with a 3% to 4% mortality in routine total hysterectomy. Any cervix, unfortunately, was premalignant. With such procedure two women in every hundred would die unnecessarily. Bland Sutton said that at least 1% mortality might be expected from embolism alone not to mention hæmorrhage, intestinal obstruction, bladder and ureter injury *et cetera*. There could be no compromise with malignant disease, but with premalignancy it was a question of making the punishment fit the crime. He personally tried to follow Bonney's practice. As one surgeon had said, "they might be able to cure a post-operative cancer, but they could not cure a post-operative death". He had no personal regrets at having done total hysterectomy, but what applied to the gall-bladder might apply to the uterus. The older surgeons, Bonney, Blair Bell, and others, had conservative minds, and they in Adelaide might not be unwise in following them.

The radiation of premalignant conditions by radium needles *et cetera* had been done for many years, and there was much to be said for it.

Fourthly, regarding Wertheim's hysterectomy, although it was very gratifying to see his own patient without recurrence three and a half years after a Wertheim's operation, it must be admitted that it was a serious operation with a high mortality. His own view was, do it, but try to select the cases carefully. Radium and X rays might be combined or used alone in inoperable cases.

Finally, as a constructive comment, he would advise all general practitioners to equip themselves with a cautery, or diathermy apparatus, and to try to keep low the incidence of pathological changes of the cervix. Also he would encourage the systematic gynæcological examination of middle-aged women, which, he thought, could be done without causing a cancerphobia.

Dr. Beard showed a patient upon whom, three and a half years ago, he had performed a Wertheim hysterectomy for cancer of the cervix. She was then aged twenty-three years, a married *nullipara*. She still felt well and there was no recurrence to be found.

DR. BRIAN SWIFT thanked Dr. Matters for his excellent paper and for all the trouble he had taken in arranging such an interesting demonstration. Dr. Swift said that the first part of Dr. Matters's paper consisted of many subjects which were controversial. He said that there appeared in nearly every journal papers on some new hormone, and it was difficult to keep up with the literature on the subject. Dr. Swift could not follow Dr. Matters's reasoning when he said that a patient was malignant when he found prolan *A* in the urine. Dr. Swift mentioned that a new cure for malignant disease had been reported in which theelin, the ovarian follicular hormone, had been given in conjunction with injections of pituitary extract to patients with a malignant growth, and in some cases a cure was reported. If prolan *A* were present in the urine, then the ovarian follicular hormone would have been formed by the action of the prolan on the ovary, and the patient ought really to be curing herself. In regard to the treatment of cervicitis, in which Dr. Matters rather stressed the treatment by coagulation by diathermy, Dr. Swift said he preferred to treat these patients by the electric cautery. With diathermy the operator was never quite certain as to the depth of the coagulation, and in many cases far too much tissue had been coagulated. Dr. Swift said that the apparatus for using the actual cautery was not expensive, and even a motor car battery could be used. The treatment by operation of lacerated cervices had been practically given up and the lacerations had been healed by cautery applications. Dr. Swift strongly condemned the treatment of cervicitis by means of radium needles, as mentioned by Dr. Matters, in conjunction with diathermy. He said that in young women the result of even small doses of radium on the ovaries was often very upsetting to their menstrual life, and with the doses used by Dr. Matters marked effect on the ovaries would result. Radium should never be used, except as a last resort. Dr. Swift said that years ago Curtis had treated cervicitis with radium and had found that menopausal symptoms often appeared after such treatment, and also that the discharge for which the patient had come for treatment persisted very often for months and months. Luckily, since that time Dickinson had discovered the cautery treatment, which gave such excellent results.

DR. RUPERT MAGAREY thanked Dr. Matters for his interesting paper, on which he must have spent a great deal of time, labour, and thought, but he felt that he could not quite agree with all that the writer had stated.

He agreed with Dr. Swift that there were hardly sufficient grounds for deciding that a woman was developing epithelioma in her *cervix uteri* simply because she was

passing prolan *A* in her urine. A great deal more work had to be done before such a statement was accepted, and the whole matter of endocrinology was so interwoven and complicated that dogmatism was impossible.

He also thought that the fine-wired electric cautery was better for use in infected and eroded cervices than diathermy. For the last few years he had used it extensively, almost to the point of eliminating the old trachelorrhaphy and cervical amputation operations, which were, in his opinion, sources of real anxiety because of the possibility of secondary hæmorrhage. But there still remained those cases of cervical infection causing absorption into the bases of the broad ligaments (? lymphatic), which was such a common source of severe chronic pelvic pain and tenderness—more particularly tenderness—and for which, frequently, panhysterectomy was the only cure. This led him to the question of total or subtotal hysterectomy. First of all, it appeared to be necessary to define terms. For example, he had recently found that a well known gynæcologist considered that the operation which in Adelaide was known as Worrall's hysterectomy, namely, the coning out of the cervical mucous membrane down to and including the external os, to be a total hysterectomy. In his own meaning, total hysterectomy meant the removal of the whole uterus. Worrall's hysterectomy was an excellent operation, but he doubted whether it quite filled the bill for those cases of acute pelvic tenderness which he had just mentioned. Moreover, so many of these patients with infected cervices suffered, after subtotal hysterectomy, from a persistent and annoying leucorrhœa that he found that he was more and more frequently performing total hysterectomy when any form of hysterectomy was required. He thought the risk of the development of epithelioma in a cervical stump was exaggerated; he could not remember seeing more than five, and in one of these he felt sure that the subtotal hysterectomy had been performed to stop hæmorrhage, which was really coming from the cervical epithelioma.

He did not think that this was the time or place to discuss radium treatment as opposed to Wertheim's operation for epithelioma of the cervix; he had gone into the question fully for the Cancer Committee recently, and hoped to publish a report, accompanied by figures, in the near future.

DR. S. L. DAWKINS drew attention to the recent discussion at the centenary meeting in London, when it was shown that radium treatment for cancer of the uterus was growing in favour, whilst there were still many surgeons, led by Victor Bonney, who advocated the complete operation. Surely, if radium was being used so successfully for a definite cancerous condition, it did seem very drastic treatment to remove the uterus for the so-called precancerous condition, and in his opinion, with the limited amount of evidence brought forward, it was not warranted.

He congratulated Dr. Matters on his paper, which had entailed much labour and research.

DR. LLEWELLIN DAVEY thanked Dr. Matters for his address and said that one of the points arising out of it for the general practitioner would be whether to advise operation or radium for cancer of the cervix.

The teaching now at most centres in England, especially the Marie Curie Clinic in London, and also on the Continent, was that the use of radium was preferable to operation, the five-year results being equal to the best surgical statistics. But also one could not help being impressed with the completeness of the radical Wertheim operation as done by Victor Bonney. However, for the majority of surgeons radium at present probably held out the best chance of success.

DR. T. G. WILSON thanked Dr. Matters for his paper, which had evidently taken up a lot of time to put together.

He did not intend to discuss the first part of the paper except to point out the danger of generalizing from so few cases. In this instance he thought Dr. Matters had detailed only two cases from which he drew his deductions.

In regard to the second part of the paper, namely, the advisability of removal of the cervix in all cases, he was doubtful of the necessity for this. In the hands of an expert the complete removal of the uterus was often a more difficult operation and liable to an increase in the mortality rate. When the cervix was involved as a result of the old inflammatory trouble, the coning out of the endometrium after Worrall's method seemed to do all that was necessary without an appreciable increase of operative risk. As regards the occurrence of cancer in the stump left after supravaginal amputation, in an experience of over thirty years he had seen only three definite cases of this condition, and from the number of patients who had passed through his hands in these years he was inclined to think it was not so frequent as some authorities claimed. In many cases when the cervix was possibly suspect, he had done the total operation as a routine, but in the ordinary case of fibroid, especially in *nulliparæ*, he had been accustomed to do merely a supravaginal hysterectomy. He felt that the added risk for the total operation was greater than the gain (in the anticipation of possible later malignancy in the stump of the cervix) warranted.

In reply to Dr. Beard, Dr. Matters said that he thought the attitude of avoiding any scientific advancement which was 100% perfect was not going to assist diagnostic investigation. After all, pathological sections went through phases of discrepancies, and although the Hofbauer method was not by any means proved to be conclusive, yet, if a cervix appeared to be premalignant clinically, then the injection of urine from the patient into a laboratory animal did not harm the patient, and if the result of the test were positive, then a total hysterectomy was not such a dangerous task as it would be to wait perhaps for a few months and then to do a Wertheim operation. In other words, they desired to discover malignant conditions before they had developed to the degree of malignant invasion.

No statement was made regarding a conflict with the opinion of Dr. Bull and the Hofbauer method. It was pointed out that before even such an authority as Dr. Bull could detect cancer by biopsy, it might conceivably be done by the Hofbauer method. The surgical zeal did not require surgical judgement, because the method mentioned reduced the radical surgery very much indeed. In a series of thirty total hysterectomies taken *seriatim*, there was no mortality and no morbidity greater than might result from any laparotomy. Dr. Matters had always preached conservative surgery, but indications must be viewed in their right perspective.

Dr. Beard mentioned malignant disease in infancy and in old age as reasons why these tests should not be made. This, after all, was begging the question, and, as mentioned by Seitz and Wintz, there was excess of prolan in the case of the infant who had uterine carcinoma as reported by them.

"We must agree with Dr. Beard", said Dr. Matters, "and not allow these investigations to cloud our clinical vision." Dr. Beard said that De Lee's immediate suture was ideal. That was indeed true, but Dr. Matters thought that, especially in obstetrics, they should aim at the ideal. It was their fault as practitioners if they allowed the public to pay ridiculously small fees for confinements relative to the fees paid for surgical measures. Dr. Matters agreed that ante-natal and post-natal care should be adequately paid for.

With regard to the 3% to 4% mortality, Dr. Matters pointed out that subtotal hysterectomy gave a 3% mortality, and simple laparotomy gave over 1%. The main thing was to have correct surgical indications. The 0·5% occurrence of cancer in the cervical stump had gone much further than this. In several series of cases compiled by Schlink it had reached over 6%, which more than offset the 4% mortality, and this, after all, was only 1% more than the mortality for the subtotal operation. Charles Mayo had collected 99 cases of cancer in the cervical stump. Apart from this, some degree of mortality occurred from many of the lacerated and infected stumps if they were not removed, and James Young said that much ill health might result from these cervices.

In reply to Dr. Swift, Dr. Matters agreed with the use of the cautery and was not a sponsor of diathermy as against the cautery, except for its ease of use and the better treatment of endocrinal infections thereby. The

diathermy had the advantage of destroying deeper tissue, as Dr. Swift stated, but the advantage was because the cautery frequently merely produced sclerosis over deep infective tissue, which continued its cryptogenic intoxication.

Dr. Matters said that he wished to correct the impression that prolan caused carcinomata. He had stated that Hofbauer had produced cervical epithelioma by injections of prolan which had presumably acted through other endocrine mechanism. Dr. Matters did not attribute any great importance to the treatment of cancer by theelin, and even if this were so, it was not the same thing as the anterior pituitary secretion.

Dr. Matters pointed out that treatment of cervices with radium needles was done in only selected cases near the menopause, and that they were of the clinically pre-malignant type. He said that it was not the Curtis method of treatment of cervicitis, as the cervicitis was first treated by cautery or diathermy, but the radium needles were placed as a halo in the cervical tissue of these bulky cervices and discharge did not remain for long.

Dr. Matters, in reply to Dr. Magarey, pointed out that sufficient time had not yet elapsed for them to see the results of treatment of the cervix with the cautery as against trachelorrhaphy or the Sturmdorf operation.

The reference to X ray cross fire with radium was in regard to X ray treatment while the radium was *in situ*. Radium needles were not recommended as a form of treatment for cancer by Dr. Matters; he merely referred to the Curtis methods. Dr. Matters thought that better results were obtained from Regaud's method with a colpostat and radium in the uterus.

In reply to Dr. Magarey, Dr. Matters said that he had made endocrinological investigations into gynæcological conditions for the past eight years. The evidence submitted here was undoubtedly slender, but it was a beginning in this direction, and the actual number of cases in which biopsy and animal investigational work had been done was now becoming a series. Dr. Matters had done seventy Siddall's tests for the œstrin in the blood of pregnant women, and several hundreds of the Aschheim-Zondek tests, quite apart from the Hofbauer reaction. The one specific instance was so outstanding as to preclude cursory attention to it. Dr. Matters was not in any way dogmatizing.

With regard to the electric cautery, Dr. Matters felt that the Nabothian follicles and infected cellular tissue far up the cervical canal was often better coagulated than cauterized, but actually there were cases in which cervical enucleation or amputation of the Sturmdorf type should be done.

Dr. Matters was very pleased to learn that Dr. Magarey agreed with him in regard to total hysterectomy. The Worrall type of hysterectomy had been sponsored, but several cases of subsequent hæmorrhage had been reported.

The incidence of carcinoma in the cervical stump had been referred to earlier, and the evidence was most startling.

Dr. Dawkins had stated that the tendency for the treatment of cancer was by radium. Forsdyke, of London, who had done more gynæcological irradiation than most men, said that more and more men were using radium, and yet he despaired at times of the results. Radium had been called the goal of the surgically dead. It was far easier to use radium than to perform radical operations, but in good hands the latter had much better five-year cases. In fact, Bonney's figures left all radium figures in a very poor state. Dr. Davey said that the five-year results of the Marie Curie Clinic were equal to the best surgical statistics. This was quite incorrect, as Heyman, of the Radiumhemmet at Stockholm, had the best radium figures, and the Bonney five-year cure was far higher than these figures.

Dr. Matters reiterated that, given uterine mobility and a satisfactory condition of the patient, he would recommend radical hysterectomy rather than radium, provided an expert surgeon were available, and he would feel that he had given the patient the best advice.

Dr. Matters said that he wished to thank Dr. T. G. Wilson for his comments because the wisdom of experience was behind him. Dr. Matters had seen the Worrall method of enucleation, and thought it very good, except that it did not remove the squamous epithelium which might become cancerous; also the subsequent discharge and morbidity of the cervix was not always overcome by Worrall's method, although most of the infected cellular tissue was removed.

NOMINATIONS AND ELECTIONS.

THE undermentioned has been nominated for election as a member of the New South Wales Branch of the British Medical Association:

Rundle, Francis Felix, M.B., B.S., 1933 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Correspondence.

CANCER OF THE UTERUS.

SIR: In THE MEDICAL JOURNAL OF AUSTRALIA dated May 6, 1933, there is a paper entitled: "Experiences in Radiation in Cancer in the Female Pelvis", by Dr. Constance E. D'Arcy and Dr. Leila Keatinge. In it is printed the following sentence: "Dr. E. T. Thring, at a recent meeting of the Section of Gynæcology and Obstetrics of the New South Wales Branch of the British Medical Association, stated that his mortality rate after the Wertheim operation was 3%." I fear that my paper must have had a deeply somnolent effect upon both Dr. Constance D'Arcy and her colleague.

I have never once followed Wertheim's method of dealing with uterine cancer. Up to 1894 I had used the vaginal method for removal of a cancerous uterus. I then realized that this method was utterly unscientific and inefficient, and in December, 1895, I operated by the "vagino-abdominal" method, which I have used ever since, improving the details of technique as experience indicated. The first case is mentioned in the paper referred to above.

Yours, etc.,

Sydney, May 8, 1933. EDWARD T. THRING.

COAL MINER'S LUNG.

SIR: One reads with amusement the scathing attack upon the radiography of the chest by Dr. Badham and Dr. Taylor in their paper entitled "Coal Miner's Lung".

The statement that "radiography of pulmonary fibrosis has lacked correction in the *post mortem* room" is neither original nor correct. The original complaint that "the radiologist needed the salutary lessons of the dead house" savours more of the epigrammatic and its criticism is more incisive. It is not correct, in this respect, that on the Silicosis Commission alone, whenever a death should occur, of any man even suspected of pulmonary fibrosis, every effort is made to obtain a *post mortem* examination, while for years *post mortem* examinations were carried out on every available case at Broken Hill.

A charge is levelled at the radiologist that he is not "competent to diagnose tuberculosis in a lung, the seat of dust fibrosis". This might be the more seriously taken to heart if it were made by an expert physician or radiologist to whom the radiological appearances of a lung in its various states of pathology were not completely unknown. This rather rabid outpouring of charges against the radiologist would appear to be unjust; unjust because the radiology of the chest remains probably the most important clinical factor in its examination, and also that estimation of disability in men, sick of dust diseases in the chest, can be made with more certainty from the radiological appearances than any single clinical factor.

With reference to the analytical findings of these gentlemen, I would like to compliment them upon work evidently most carefully and laboriously performed, though, as a radiologist, I cannot comment on their value.

Yours, etc.,

H. M. CUTLER.

Macquarie Street,
Sydney,
May 12, 1933.

GASTRO-ENTERITIS.

SIR: In your issue of March 25 there appears an article by Dr. Lindsay Male, which we have read with the greatest interest, and, in perusing this article, we notice that mention of the use of "Lactone" syrup is omitted.

Many members of the medical profession have had very successful results with lactic acid feeding per medium of "Lactone" syrup, including Dr. Male, and we feel sure you will be able to find space in your valuable publication for this communication, drawing attention to the fact that the principal successes with lactic acid feeding have undoubtedly been due to the use of "Lactone" syrup.

Yours, etc.,

F. H. FAULDING AND COMPANY, LIMITED.
(W. Brendon Garner, Director.)

Perth, Western Australia,
April 21, 1933.

"D.H.A. GUIDE TO THE BRITISH PHARMACOPŒIA, 1932."

SIR: We are indebted to a young South Australian pharmacist for bringing under our notice an error in the monograph on *syrupus scillæ* in the "D.H.A. Guide to the British Pharmacopœia".

In the compilation of the guide, the percentage of *acetum scillæ* of the 1914 issue was wrongly taken as v/v, whereas, as a matter of fact, it is the unusual and rather irrational basis of v/w. It followed from this that the comparisons which were made between the old and the new syrups of squill were correspondingly in error.

Although the error is not likely to perturb any physician or practising pharmacist, we are aware that the guide is being widely used throughout the Commonwealth in the training of students, and it is primarily because of this that we ask the courtesy of your columns to publish the following correction.

The monograph on page 79 should properly read as follows:

SYRUPUS SCILLÆ.

45 per cent. v/v of the new Vinegar of Squill replaces 15 per cent. v/w of the old formula. The new Vinegar of Squill is approximately half the strength of the old, and, allowing for the difference in the methods of computing the percentages in the 1914 and 1932 issues, the new Syrup of Squill is approximately one-fifth weaker in Squill than the Syrup of the 1914 issue. The Refined Sugar is slightly decreased.

The dose remains unaltered.

Yours, etc.,

DRUG HOUSES OF AUSTRALIA, LIMITED.

May 12, 1933.

AN ECONOMIC COMMENTARY AND DIAGNOSIS.

SIR: Dr. Paul Dane's letter on the economic question would be amusing if the issue were not so tragic. Every economist or even banker who has appeared in the limelight, has admitted that the disease is a deficiency of purchasing power. The cure is obviously to locate the error or errors in the body economic which are the cause of this condition. Of the errors it is also necessary to define the key, or basic, error. This Major Douglas has done.

Whilst to Henry George must be awarded due honour and appreciation for his great contribution to economic thought, his analysis, though quite humane in intent, was applied to a period before the mechanization of industry was so advanced, and before the wholesale monopoly of the issue of financial credit (money) was so universally centralized and deeply entrenched.

Henry George and those of his followers whom I have met do not appreciate the relation and power of the money or distributing section of economics. Banking and the creation and destruction of money are apparently not of prime importance in his analysis. Now, money being a legitimate title of claim to the goods on sale, and being also the modern method of distribution of goods, it is apparent that the removal from private corporations of their monopoly of money manufacture is the first step which a nation must take in order that economic distribution may become a national function.

The application of science to industry has changed the functions of money. Formerly money was primarily the means by which producers exchanged goods and services, and it was necessary for nearly everyone to produce or serve for gain. But now that scientific industry needs fewer and fewer workers, who have nothing to do with marketing their goods, the actual function of a money system is distribution.

Unemployment can never again be cured by employment.

Dr. Dane says that three inquiries have discarded the ideas of Major Douglas. This may be true, but it must be remembered that the financial monopoly, the universal spiderweb of Wall Street, will fight by fair means or foul in order to prevent its usurped power to create money being wrested from it. The personnel of those committees of inquiry should be carefully considered, when it will be seen that the money power pervaded them, insuring that their findings would inevitably deny what finance only too well knows to be the cure for the crisis. Money Moloch's lions are abroad chewing up social credit propagandists everywhere, and a sane solution of our economic problem can be hoped for only from a nucleus of our intelligentsia, with the will, determination, and faith which can remove mountains and tame lions.

Dr. Dane states that the controllers of three businesses have told him that they dispense purchasing power equal to the prices of the goods which they produce. If they get in only as much as they pay out, why the effort of producing? And have they no depreciation charges, in respect of plant purchased in the past, which must be added to the prices of goods produced in the present?

The A + B theorem, which his mathematician declares to be wrong, is thus stated by Douglas:

> In any manufacturing undertaking, the payments made may be divided into two groups: Group A, payments made to individuals (wages, salaries and dividends); Group B, payments made to other organizations (raw materials, bank charges and other external costs). The rate of distribution of purchasing power to individuals is represented by A, but since all payments go into prices, the rate of generation of prices cannot be less than A *plus* B. Since A will not purchase A *plus* B, a proportion of the product at least equivalent to B must be distributed by a form of purchasing power which is not comprised in the description grouped under A.

A moment's consideration will show that this theorem is self-evident and quite unarguable. Whatever it was that the mathematician declared to be wrong, it could not have been the A *plus* B theorem as stated by Douglas, although it may conceivably have been Douglas's A *plus* B theorem as stated by someone else. The theorem is stated and its implications fully discussed in Douglas's book, "The Monopoly of Credit", in Chapter Four, to which I refer Dr. Dane. This chapter establishes beyond all reasonable doubt that the rate of flow of purchasing power in each and every industry must inevitably be less than the rate of flow of price. Price is the relation of money to goods, therefore a full knowledge of the life cycle of money is necessary to a full insight into the A *plus* B theorem.

Monopoly of the means to produce is, of course, important; but the monopoly of the means of distribution (money) is more easily acquired and is equally efficacious in reducing the people of the world to subjection. In any case, all that Henry George sought is embraced in Major Douglas's draft scheme for Scotland.

In conclusion, I suggest that, before again expressing condemnation of the genius of Major Douglas, Dr. Dane should ask himself the following questions: What is the nature, source and origin of money? How much money should be in existence at any given time? What is the function, mechanism, and life cycle of money? Who should have the right to create and destroy money?

Yours, etc.,

"M.D., C.M."

May 15, 1933.

Obituary.

ROBERT DOUGLAS BRUMMITT.

WE regret to announce the death of Dr. Robert Douglas Brummitt, which occurred on May 21, 1933, at St. Peters, South Australia.

Books Received.

CLINICAL OPHTHALMOLOGY FOR HOUSE SURGEONS AND STUDENTS, by J. M. Bickerton, M.A., B.Ch., F.R.C.S., and L. H. Savin, M.D., M.R.C.P., F.R.C.S.; 1933. London: H. K. Lewis and Company, Limited. Demy 8vo., pp. 165, with 92 illustrations. Price: 7s. 6d. net.

VITAMINS AND OTHER DIETARY ESSENTIALS, by W. T. Aykroyd, M.D.; 1933. London: William Heinemann (Medical Books) Limited. Demy 8vo., pp. 218. Price: 7s. 6d. net.

WHITLA'S PHARMACY, MATERIA MEDICA AND THERAPEUTICS; Twelfth Edition; Revised by J. A. Gunn, M.A., M.D., D.Sc., F.R.C.P. *et al*; 1933. London: Baillière, Tindall and Cox. Crown 8vo., pp. 657, with illustrations. Price: 12s. 6d. net.

Diary for the Month.

JUNE 7.—Victorian Branch, B.M.A.: Branch.
JUNE 7.—Western Australian Branch, B.M.A.: Council.
JUNE 9.—Queensland Branch, B.M.A.: Council.
JUNE 13.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
JUNE 20.—New South Wales Branch, B.M.A.: Ethics Committee.
JUNE 21.—Western Australian Branch, B.M.A.: Branch.
JUNE 22.—New South Wales Branch, B.M.A.: Clinical Meeting.
JUNE 23.—Queensland Branch, B.M.A.: Council.
JUNE 27.—New South Wales Branch, B.M.A.: Medical Politics Committee.
JUNE 28.—Victorian Branch, B.M.A.: Council.
JUNE 29.—South Australian Branch, B.M.A.: Branch.
JUNE 29.—New South Wales Branch, B.M.A.: Branch.

Medical Appointments.

Professor J. B. Cleland (B.M.A.) has been appointed a Member of the Advisory Council of Aborigines, South Australia.

Medical Appointments Vacant, etc.

For announcements of medical appointments vacant, assistants, *locum tenencies* sought, etc., see "Advertiser", page xvi.

CHILDREN'S HOSPITAL (INCORPORATED), PERTH, WESTERN AUSTRALIA: Junior Resident Medical Officers (male).
HOBART PUBLIC HOSPITAL, HOBART, TASMANIA: Junior Resident Medical Officer.
LAUNCESTON PUBLIC HOSPITAL, LAUNCESTON, TASMANIA: Resident Medical Officers.

Medical Appointments: Important Notice.

MEDICAL practitioners are requested not to apply for any appointment referred to in the following table, without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

BRANCH.	APPOINTMENTS.
NEW SOUTH WALES: Honorary Secretary, 135, Macquarie Street, Sydney.	Australian Natives' Association. Ashfield and District United Friendly Societies' Dispensary. Balmain United Friendly Societies' Dispensary. Friendly Society Lodges at Casino. Leichhardt and Petersham United Friendly Societies' Dispensary. Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney. North Sydney Friendly Societies' Dispensary Limited. People's Prudential Assurance Company Limited. Phœnix Mutual Provident Society.
VICTORIAN: Honorary Secretary, Medical Society Hall, East Melbourne.	All Institutes or Medical Dispensaries. Australian Prudential Association, Proprietary, Limited. Mutual National Provident Club. National Provident Association. Hospital or other appointments outside Victoria.
QUEENSLAND: Honorary Secretary, B.M.A. Building, Adelaide Street, Brisbane.	Brisbane Associated Friendly Societies' Medical Institute. Chillagoe Hospital. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL are advised, in their own interests, to submit a copy of their agreement to the Council before signing. Lower Burdekin District Hospital, Ayr.
SOUTH AUSTRALIAN: Secretary, 207, North Terrace, Adelaide.	Combined Friendly Societies, Clarendon and Kangarilla districts. All Lodge Appointments in South Australia. All Contract Practice Appointments in South Australia.
WESTERN AUSTRALIAN: Honorary Secretary, 65, Saint George's Terrace, Perth.	All Contract Practice Appointments in Western Australia.
NEW ZEALAND (Wellington Division): Honorary Secretary, Wellington.	Friendly Society Lodges, Wellington, New Zealand.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

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